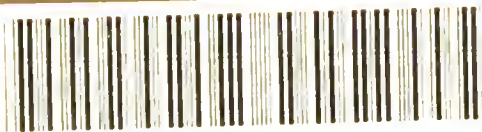


ANTIPYRIN

(Dr. KNORR.)



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# SCIENTIFIC · REPORTS

ON

# ANTIPYRIN

(DR. KNORR),



COLLECTED FROM THE PRINCIPAL MEDICAL  
PUBLICATIONS OF THE WORLD.

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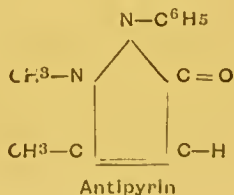
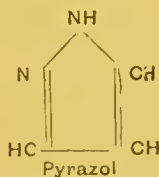
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# PREFACE.



FOR upwards of five years a new chemical product has been very successfully used as a medicament all over the world, for the discovery of which Science is indebted to the researches of Dr. Knorr on Pyrazole.

The substance is now called Antipyrin on account of its antipyretic properties. It is produced by the action of phenyl-hydrazin on acetic ether, and the subsequent methylation of the product. Its composition corresponds to the formula ( $C_{11}H_{12}N_2O$ ) and its constitution may be indicated by the designation of Dimethyl-phenyloxypyrazol, or by Dimethyl-phenyl-pyrazolon. This constitution, according to the elaborate researches of its discoverer, is seen in the formula grouped as follows :—



Antipyrin as it is found in commerce is an artificial alkaloidal base in the form of a white crystalline powder, or in scales, remarkable for its ready solubility in water. Its most characteristic reactions are those it gives with perchloride of iron and nitrite of

soda; the former produces a deep reddish brown colour in the neutral solution, the latter an intense emerald green tint in the slightly acidulated solution.

Antipyrin is now one of the most important articles of *Materia Medica* extant, for the treatment of various diseases. When first brought out it was supposed to be merely an antipyretic, but since then it has been proved to possess so many further valuable properties, chief amongst which is its inestimable value as an analgesic or painkiller, that it is now considered one of the most universally active remedies. Since its introduction very much has been written about it by different medical men, and the collected papers would fill thick volumes.

In employing a drug it is necessary that a medical man should know all the details of the various methods for using it, and the degree of success others have obtained. The object of this work is to lay before the medical profession this information as regards Antipyrin. It consists of a series of reports of various authors on their researches, and may be termed a compendium of the properties, action, and administration of this remedy. It is unnecessary to say that only such papers have been quoted as contain original matter, since it would be of no use to repeat from a fresh author the same truth in another form.



# SCIENTIFIC REPORTS

ON

## ANTIPYRIN

(DR. KNORR),

COLLECTED FROM THE PRINCIPAL MEDICAL PUBLICATIONS OF THE WORLD.



**From the Clinic in Erlangen.**—On ANTIPYRIN, a new antipyretic, by Prof. Dr. WILHELM FILEHNE, of Erlangen (*Zeitschrift für Klinische Medicin*, Bd. VII., H. 6).

Filehne discovers that the substance called Antipyrin possesses powerful antipyretic properties. The action sets in gradually, lasts from 5 to 18 hours if a sufficiently strong dose has been given, and passes off gradually. For adults a quantity of 75 to 90 grains is amply sufficient for reducing fever temperature, even in its highest degree, to the nearly normal temperature of 100°. The said quantity is best divided into three single doses, each of which is administered at one hour's interval from the other (30+30+15 grains, or 30+30+30 grains, 6+6+3 Tabloids, or 6+6+6 Tabloids). After being reduced the temperature remained low for some time, the duration of which varied much with different patients. Generally, after 7 to 9 hours—sometimes only after 18 or even 20 hours—the temperature gradually rose again. The rise and fall were always gradual—the former was usually not accompanied with profuse perspiration, the latter never set in

with rigor. Unpleasant after-effects were not observed, occasional vomiting excepted.

For children, half the dose indicated above is sufficient. Smaller doses are, according to Professor Filehne, indicated for phthisical and very emaciated patients.

Antipyrin is, according to Filehne, best prescribed in powders of 15 or 30 grains (3 to 6 5-grain Tabloids), (7 or 15 grains for children), which, for each administration, are dissolved in water (with or without the addition of a corrigens) or in wine.

Frequently repeated small doses did not seem to have such a good effect as a few large doses with short intervals between each. One very large single dose had not such a good effect as the same dose split into several divisions, and had the disadvantage of producing vomiting.

Filehne made extensive experiments first on animals, then on man in health as well as in disease. He minutely recorded the course of temperature on about 100 dogs in the various acute and chronic febrile disorders. His latter observations were made at the Civil Hospitals of Nürnberg and Moabit (Berlin).

**From the Civil Hospital Moabit in Berlin.**—On the action of ANTIPYRIN, by Dr. PAUL GUTTMANN, Medical Superintendent and University Lecturer on Therapeutics (*Berlin. klin. Wochenschrift*, 1884, N. 20).

The author entirely confirms Filehne's statements on Antipyrin. The results of his experiments show that Antipyrin forms a most reliable and very powerful antipyretic remedy. He likewise recommends to split the dose of 60 to 90 grains into 2 or 3 single doses of 30 grains each (6 Tabloids). The powders are given in wafer, or dissolved in water, with the addition of some substance to cover the taste. The abatement of temperature is continuous and gradual. Only one hour after the first dose has been given a falling of 1° is noticeable. During the second hour after the dose has been repeated a further fall takes place, the maximum of abatement is reached during the third or fourth hour, especially if in the meantime a third dose of 15 or 30 grains (3 to 6 Tabloids) has been administered. The least abatement noticed was

3°; the utmost 6°; 4° abatement was very frequent. The duration of the effect, *i.e.*, the time between the maximal abatement and the re-rising of the temperature, varied greatly in the different cases. It amounted to at least 5—6 hours, sometimes to 12 or even 18 hours. The effect of Antipyrin is so much prolonged because the consecutive rising of temperature is very slow and gradual, and never accompanied with rigors, the latter in contradistinction to kairin. The maximum of abatement with Antipyrin lasts only a short time—about 1—2 hours.

The author considers the dose indicated above the most appropriate for obtaining a powerful and lasting effect. Similar effects may be obtained by administration of one single dose of 60 grains, or by giving small doses of 15 grains each, repeated every hour for about five times. Further division of doses produces uncertain effect. Concomitant with the abatement of temperature is a lessening of the frequency of the pulse.

The action of Antipyrin is without unpleasant after-effects. Only in a few cases vomiting is observed, otherwise Antipyrin is well borne. Where the falling of temperature is very considerable, profuse perspiration is sometimes noticed.

**From the St. Catherine Hospital at Stuttgart.**—On the therapeutic value of ANTIPYRIN, Dr. C. RANK (*Deutsche med. Wochenschrift*, 1884, N. 24).

The author tried Antipyrin about 50 times, on 35 different people.

He first proceeded exactly like Filehne and Guttman, gave 30 grains (six 5 gr. Tabloids) three times, with one hour's interval between each dose. But so far he was not quite satisfied, as in some patients, especially delicate women, the drug was sometimes vomited. He therefore resorted to subcutaneous application, which he tried in 25 cases. Antipyrin is soluble in hot water, according to the proportion of 1 :  $\frac{1}{2}$ . On cooling, this solution preserves its strength, and is therefore very suitable for injection. From 15 to 20 minims of the solution produced a powerful antipyretic effect. The injections were mostly made in the gluteal region, where they did not cause any local irritation,

except some slight tenderness, lasting only a short time, localised to the point of insertion of the needle. Nausea or vomiting never occurred after these subcutaneous applications.

Considerable and sudden abatement of temperature was accompanied with profuse perspiration; subsequent increase of the temperature was always gradual and without rigor. In one case the author observed an eruption resembling nettle-rash appearing half-an-hour after injection, quickly spreading over the whole body, and disappearing again rapidly.

The author draws the following conclusions:

(1) Antipyrin is an efficacious and reliable antipyretic in all cases of febrile disorders. It is without any disagreeable secondary effects.

(2) Subcutaneous application of Antipyrin produces a more rapid and more considerable abatement of temperature than internal administration; the necessary dose is much smaller with the former, one single dose of 30 grains (six 5 gr. Tabloids) being generally sufficient.

(3) A concentrated solution 200 per cent. is most suitable for subcutaneous injection. This application is not accompanied by any local or general disturbances.

(4) The subcutaneous administration is preferable to the internal and to the application per rectum, except where a rapid falling of the temperature might do harm, as with very emaciated weak patients and with children.

(5) Advantages of the subcutaneous method:

(a) half or a third of the ordinary dose is sufficient.

(b) vomiting is avoided.

**From the Internal Clinic of the University of Königsberg.**—Under direction of Prof. NAUNYN. On the action of ANTIPYRIN, by Dr. FALKENHEIM (*Berlin klin., Wochenschrift*, 1884, N. 24).

The author confirms Filehne's and Guttman's statements given in doses of 30+30+15 grains at intervals of one hour. Antipyrin invariably reduced the temperature. The amount of reduction was usually 4° to 6°, sometimes more. It generally was gradual,

as was also the subsequent rise; the latter was never accompanied by rigor. One hour after the first dose an abatement of  $1^{\circ}$  was usually observed; sometimes, especially with anæmic patients, this first abatement was  $4^{\circ}$ , once even  $6^{\circ}$ . Sometimes the effect was retarded until the third dose had been given. The author thinks that more or less rapid absorption is the cause of these variations. The effect of the three customary doses lasted about five hours, and was sometimes even noticeable on the following day.

The abatement of the fever was associated with a reduction of the frequency of the pulse. Moderate perspiration took place where the effect was rapid. Besides occasional nausea, no bad after-effects were noticed.

The author declares that Antipyrin forms a valuable substitute for Quinine in all cases of febrile diseases (malaria excepted), where a speedy and reliable reduction of temperature is desirable.

**From the Civil Hospital of Cologne.**—ANTIPYRIN, the latest antipyretic. Paper read before the Medical Society of Cologne, on the 26th May, 1884, by Dr. FERD. MAY (*Deutsche med. Wochenschrift*, 1884, N. 24—27).

The author treated 22 cases of high fever with Antipyrin. In each case under the influence of this drug he observed a prompt and rapid reduction of temperature. Falling and subsequent rising were slow and steady; the action of the drug lasted very long. The frequency of the pulse decreased in proportion with the lessened fever.

The only unpleasant after-effect of which his patients complained was more or less profuse perspiration. Vomiting occurred in seven cases. As the temperature went up slight shivering was sometimes seen, but not much to speak of; never any characteristic rigor. Collapse was seen once in a pale and emaciated patient with small and frequent pulse.

For adults, Filehne's dosage (30+30+15 grains) was found most appropriate and efficacious. With phthisical patients and children a much smaller dose, 7 to 15 grains (1 to 3 Tabloids) proved sufficient. With still smaller doses, the effect was unsatisfactory.



The author recognised the following advantages over other antipyretics :—

1. Ready solubility of the drug in water and in wine.
2. The readiness with which the slight after-taste is covered.
3. Quick and prompt action.

Several cases of severe pneumonia, where quinine had failed, were most successfully treated with Antipyrin.

**From the Clinic of Prof. Dr. Biermer.** Privy Medical Council of Breslau.—On ANTIPYRIN and its action in different fevers. Paper read before the Medical Society of Silesia, by Dr. ALEXANDER, First Assistant of the University Clinic of Breslau (*Bresl. ärztl. Zeitschrift*, 1884, N. 11).

The author treated 15 patients with Antipyrin. In each case he observed a rapid reduction of the temperature, which sometimes returned to its normal state. The average dose was 60 to 90 grains, divided into single doses of 15 or 30 grains (3 to 6 Tabloids). The falling of temperature usually set in after the first dose of 30 grains, and was accompanied by perspiration. After the last single dose had been given, the temperature remained low for a considerable time, which was longest in cases of typhoid fever (up to 15 hours) ; not quite so long in pneumonia.

*Recurrent fever* was kept at a nearly normal temperature during its whole course by one large dose of Antipyrin, followed by continuous administration of small doses. In one case of *Intermittent fever*, the fever paroxysm was checked when the drug was given as soon as the critical symptoms appeared. Recurrence of the fever was not prevented. Duration of the attack was shortened if the drug was given while the fever was at its height.

In one case of *Rheumatic fever*, pains and fever disappeared after administration of Antipyrin, but the author does not yet believe in a specific action of the preparation in the disease named. In a case of advanced *Phthisis*, with high fever, the temperature became normal, whilst the frequency of the pulse was not diminished. In other cases, abatement of temperature and decrease of the pulse were always simultaneous. Disagreeable or threatening symptoms were never observed. Vomiting did occur, but not often, and

never to such an extent that the patients refused to continue to take the medicament. Only female patients brought up the drug, and they were mostly individuals who vomited every other powerful remedy.

Rigor never occurred, and the temperature went up again very gradually.

The author unhesitatingly declares that Antipyrin is a most valuable addition to the stock of drugs, and he anticipates a general use of Antipyrin, especially in the treatment of typhoid fever and of phthisis.

**From the General Hospital at Luebeck.**—Contribution to the antipyretic action of ANTIPYRIN, by Dr. A. BUSCH, First Assistant (*Berlin klin., Wochenschrift*, 1884, N. 27).

Dr. Busch treated 9 cases with Antipyrin. It was usually given in the afternoon in doses of 30+30+30 grains or 45+45 grains. Considerable rise of temperature after the morning visit was considered an indication for prescribing the drug.

The temperature went down steadily, and mostly reached a nearly normal point after 2—6 hours. Average abatement: 4°, maximal 6°, minimal 0·8°.

The author completely agrees with Filehne in his statement, that the action of Antipyrin was absolutely certain and constant. Nausea and vomiting never occurred. Ascension of temperature was, with one exception, never accompanied by rigor. The frequency of the pulse mostly diminished in proportion with the reduction of temperature. Perspiration was of regular occurrence. It was abundant and disagreeable where a previous predisposition (Phthisis) existed. Otherwise the patients liked the medication, and did not object to its continuance.

According to the author Antipyrin will, in consequence of its prompt and reliable action, have a great future as an antipyretic.

**From the Civil Hospital Moabit in Berlin.**—"On ANTIPYRIN." A paper read before the Berlin Medical Society, on the 14th July, 1884, by PAUL GUTTMANN, med. director of the hospital (*Deutsche med. Wochenschrift*, 1884, N. 31). After his first publication on Antipyrin (cf. *Berl. klin. Wochenschrift*, 1884, N. 20),

the author continued his researches, and his present experience is now based on 122 trials with 60 patients.

Antipyrin given in a quantity of 60 to 75 grains divided into three doses of 30+15+15 (6+3+3 Tabloids), or 30+30+15 grains (6+6+3 Tabloids) respectively, which were administered at one hour's interval from each other, never failed to produce a considerable reduction of the febrile temperature, the effect lasting for 5, 6, often for 10 hours, and sometimes still longer. Similar was the action of one single dose of 60—75 grains. Doses of 15 grains were also efficacious, but had to be repeated every hour. Smaller doses given at shorter intervals did not do much good, except with children, where doses of 10 (2 Tabloids) grains, repeated several times, proved sufficient.

Uninterrupted falling of the temperature was seen when the dose consisted of 30+30+15 grains, with one hour's interval between each single dose. After three or four hours, the maximal abatement was attained. It amounted to at least 3°, mostly over 4°, sometimes 6° or even 8°. If only an abatement of 3° is intended, it will be found sufficient to give 30 or 45 grains twice.

After the maximum of reduction was reached, the temperature slowly and gradually rose to attain its former height, only after 10, 12, or even 18 hours. The frequency of the pulse went down conjointly with the fever, but not quite in the same proportions.

There were no unpleasant secondary effects. Abundant perspiration was observed when the temperature fell rapidly, but this symptom did not cause any trouble. Also, the occasional vomiting was of such a slight nature that it could not be described as an unpleasant secondary effect. Re-rising of the fever did not cause any uneasiness, nor was rigor ever associated with it.

Guttmann also used subcutaneous injections of Antipyrin, which method he employed in five cases, also with children, with decided success.

**From the Internal Clinic of the University of Breslau.**—Second report on the primary and secondary effect of Antipyrin, by Dr. ALEXANDER, First Assistant (*Breslauer ärztl. Zeitschrift*, 1884, N. 14).



Since the publication of his first researches (*Breslauer ärztl. Zeitschrift*, 1884, N. 11) the author made further investigations on a more extended scale. A further number of 51 patients, suffering from different kinds of fever, were treated with Antipyrin.

With only one exception (mitral endocarditis with rheumatic fever), he succeeded in all cases in reducing the febrile temperature to its normal level, and in keeping it down for a considerable time. The necessary dose varied between 30 and 90 grains (very rarely 120—150 grains), and between 4 and 20 grains with children. With the latter, the daily quantity was divided into several single doses of 4 grains each.

In intermittent fever, Antipyrin caused lessening of the fever, but a cure was not effected. Typhoid fever seemed to be of a milder character when treated with Antipyrin.

Of secondary effects vomiting was again observed; to avoid it Antipyrin was successfully applied per rectum (dose: 30 grms.—[6 Tabloids]—dissolved in 6 ounces of water). It was also supplied subcutaneously, but this method was given up again.

Novel was his observation, that Antipyrin sometimes caused an eruption. He saw this in several cases of typhoid fever; the exanthema was itching and much resembled that of ordinary measles. It disappeared without desquamation even when Antipyrin was continued and did not cause the patient any discomfort. In one case miliaria alba of a very characteristic nature was observed after 90 grains of Antipyrin had been given. A case of typhoid fever combined with Antipyrin rash was at first mistaken for typhus.

With regard to rheumatic fever the author modifies his former statement, and believes that in this disease Antipyrin not only has an antipyretic effect, but also that it acts favourably on the affections of the joints. In six out of eight cases of acute rheumatic arthritis a speedy recovery was obtained; in one subacute, prolonged case, Antipyrin undoubtedly effected marked improvement; only once it failed to act on the joints, whilst its antipyretic effect was in evidence. In rheumatic fever the drug was given in full doses until the temperature remained normal, and

even then its use was prolonged for a few days, twice 30 grains (6 Tabloids) being given daily.

**From the Medical Policlinic in Erlangen.**—ANTI-PYRIN, in fevers of children. By Prof. Dr. PENZOLDT and E. SARTORIUS (*Berlin klin., Wochenschrift*, 1884, N. 30).

The authors used Antipyrin largely in children's affections. They prescribed it on 120 days to 21 little patients, and came to the following conclusions:—

1. Antipyrin given in febrile disorders of children is a very appropriate medication, which infallibly reduces the temperature.
2. Given in suitable doses it causes an abatement of several degrees, lasting for several hours.
3. The decrease of the frequency of the pulse does not always correspond to the reduction of the temperature.
4. The effect on the patient's general conditions is mostly favourable.
5. In undesirable secondary effects vomiting was sometimes noticed. If this should occur frequently the drug had better be given per rectum.
6. Twice as many grains as the child counts years are given as a single dose, which is repeated three times, one hour intervening between each dose. Even larger doses may be given with perfect safety if the desired effect should not have been obtained. The appropriate dose for administration per rectum is: 5—10 times as many grains as the child is old.
7. The infantile organism seemed to adapt itself to the prolonged introduction of the drug.

**From the Internal Clinic of Prof. Riegel in Giessen.**—On the action of ANTI-PYRIN. By CARL V. NOORDEN, assistant of the Clinic (*Berlin klin., Wochenschrift*, 1884, N. 32).

Antipyrin was exactly prescribed according to the rules laid down by Filchne (30+30+15 grains [6+6+3 Tabloids] with one

hour's interval between each dose). The results of other authors were fully confirmed. Abundant perspiration was the only disagreeable after-effect, which was checked by combination of the remedy with Agaricin (2 pills of  $\frac{1}{10}$  grain each) or Atropine ( $\frac{1}{80}$  grain). The antipyretic effect was not affected.

Vomiting, which seldom occurred, was completely avoided by subcutaneous application. Arterial pressure did not seem to be influenced by the drug.

**From the Berlin Charité Hospital**, under direction of Prof. LEYDEN. O. Tilmann, ANTIPYRIN, the latest antipyretic. (Diss. 8.36. Gs. Berlin).

Antipyrin was usually given internally, rarely by subcutaneous method. The antipyretic effect never failed. Intermittent fever was not cured by Antipyrin, but the attacks were shortened or altogether repressed.

In other diseases with intermittent fever curve its action was much more beneficial. In one case of cerébral abscess, for instance, where Quinine and Arsenic had failed to check the fever attacks, doses of 60 grains of Antipyrin removed rigors and fever. A similar striking result was obtained in a case of ulcerative endocarditis.

The influence on fever in phthisis was very evident. Even subnormal temperature was never accompanied by collapse.

Vomiting was observed several times, but the appetite remained good. Perspiration was regularly recorded after Antipyrin. Consumptive patients were most susceptible in this respect.

**From the Internal Clinic at Zürich.**—ANTIPYRIN RASH, by Dr. PAUL ERNST, First Assistant. (*Centralbl. für. klin. Medicin*, 1884, N. 33).

The author had occasion to use Antipyrin most extensively during a very large and serious epidemic of typhoid fever. He made comparative experiments with Antipyrin and Quinine, and came to the conclusion that, especially in cases of hectic fever where Quinine failed, a prompt and lasting remission of fever was obtained by Antipyrin. In all other respects his great experience confirmed the favourable statements of previous investigators.

Disagreeable vomiting was prevented by giving Antipyrin as enemata dissolved in water with addition of some starch.

The author subsequently reports on five cases of medicinal exanthema caused by internal use of Antipyrin. The rash observed was similar to measles, spread over the whole body, face and neck excepted. In one case it disappeared, although Antipyrin was not discontinued.

**From the Internal Clinic of Prof. Gerhardt in Berlin.**—Researches with regard to treatment with Antipyrin (*Centralblatt für klin. Medicin*, 1884, N. 36).

Doses of 15 grains and less acted unsatisfactorily. By giving 60—90 grains in the course of one or two hours even the highest fever temperature was reduced to normal. With moderate fever, and with such of hectic type, doses of 20—30 grains were sufficient. Phthisical patients, and patients in the last stage of typhoid fever, did very well with comparatively small doses. Tuberculosis of the lungs formed a valuable test for the harmlessness and usefulness of Antipyrin, because in this disease the new febrifuge medicament was taken without causing the slightest trouble, whilst other modern antipyretics had sometimes given rise to very unpleasant symptoms.

With regard to the action of Antipyrin, the author observed that twenty minutes after the first large dose the skin became moist and congested, the subcutaneous veins enlarged, and mostly a very marked perspiration set in.

The frequency of pulsation decreased moderately under the influence of the drug, arterial tension increased, and the pulse became feebler. Dicrotic and policrotic quality of the pulse, as occurring in typhoid fever, disappeared altogether. The dicrotic wave of the pulse-nerve still remained, but became smaller, and approached the primary wave. Slight præ- and post-dicrotic waves were observed.

The gradual and slow rise of the temperature curve, after Antipyrin was left off, took at least three to six hours. The usual slight after-effects, such as nausea and vomiting, did occur, but only to a moderate degree. The author twice

observed drowsiness and involuntary micturition after Antipyrin.

**From the Internal Clinic of Prof. Kussmaul in Strassburg.**—On Antipyrin and Antipyrin Rash, by Dr. A. CAHN, Assistant (*Berlin klin. Wochenschrift*, 1884, N. 36).

The author states that in Antipyrin a most reliable febrifuge has been discovered. The preparation has the great advantage of being nearly free from unpleasant secondary effects. It was usually taken without any discomfort. Vomiting occurred only in one case of advanced phthisis. The drug was usually administered between 11 a.m. and 2 p.m., in single doses of 15—45 grains (3 to 9 Tabloids). In high fever (typhoid and pneumonia), daily doses of 60—90 grains were necessary. In moderate fever (pleurisy and later stage of typhoid), and even in high fever of phthisis, daily doses of 30—45 grains (6—9 Tabloids) caused a state of complete apyrexia.

Abatement of temperature, especially with consumptive and other patients of reduced resistance, was often accompanied by profuse perspiration; but the latter never was abundant enough to justify special mediation against it. Re-rising of temperature took place without any rigor. Indifference to the action of the remedy by continued use was never observed.

The pulse was always influenced favourably, the frequency lessened, and the tension increased considerably. In typhoid fever, the secretion of urine was increased, and the specific gravity of the liquid became lower.

A medicinal rash was often observed after administration of the drug. It usually was of the kind known as erythematous, mostly confined to the dorsal aspect of the limbs. It did not cause any discomfort, and was no indication for discontinuing the use of the drug.

**Maragliano L'antipyrina; nuovo Antipyretico.**—*Gaz. degli Ospitali*, 1884, N. 72).

A solution of iodine and iodide of potassium forms the most reliable test for Antipyrin. Even if the latter is diluted to 1 in 100,000, a distinct reaction takes place (reddish precipitate).



Arterial tension increases after Antipyrin. Cutaneous circulation of blood is more rapid.

The author entirely confirms the experience of others with regard to the high therapeutic value of the drug.

**Antipyrin in cases of Puerperal Fever.**—By Dr. MAX JAHN-GREVESMUEHLEN (*Deutsche medicin. Zeitung*, 1884, N. 78).

The author reports on a case of grave puerperal fever, which was treated by administration of Antipyrin with surprising success. Filehne's method of administration (30+30+15 grms.—6+6+3 Tabloids) was followed. It was borne very well. Peritonitic pains disappeared half-an-hour after the first dose of 30 grains (6 Tabloids). The effect lasted five to six hours. The rigors disappeared after the first full daily dose, and, with the exception of one single instance (short exacerbation of peritonitis), did not reappear during the whole course of the malady. The high temperatures were regularly reduced, and the patient felt comparatively comfortable as soon as she was under the influence of the drug. Inclination to collapse was never observed.

**Contribution to the physiological and therapeutic action of Antipyrin**, by R. DEMME, of Berne (*Fortschritte der Medicin*, 1884, N. 20, 21).

Demme's therapeutic researches are based on 23 selected cases of infantile diseases treated with Antipyrin. He made very careful records, and obtained results as follows:—

Antipyrin is a very valuable antipyretic in children's affections. Up to 8° of reduction of the temperature have been recorded, which effect may begin one hour after administration. The usual time, however, is three to four hours. The complete apyrexia lasts often for 24 hours, and subsequent increase is very gradual.

Simultaneous with the abatement of temperature is a decrease in the frequency of the pulse, and an increase of arterial tension. A preliminary short increase of pulse-rate is sometimes observed.

Serious diphtheritic infection, with threatening weakness of the heart and degeneration of its muscular fibres, is a decided contraindication to the use of Antipyrin. Whenever the heart is much affected from previous illness, Antipyrin ought not to be given.

Robust children, who, up to the date of their illness have been quite strong, may take even large doses without any harm being done.

Antipyrin may also be given to unweaned infants. Appetite and digestion remained normal after its administration, and vomiting very rarely followed. With regard to unpleasant secondary effects, Antipyrin is much superior to other antipyretics of old repute, such as Quinine and Salicylic Acid. Tinnitus, drowsiness, and vertigo were never observed after the administration of Antipyrin, whilst after the use of the other antipyretics they are only too common. Increase of secretion of urine is a frequent effect of Antipyrin.

In 3 out of 23 cases the often-described Antipyrin rash has been observed. It commenced several days after the first dose had been given, and lasted five days at the most.

**On Antipyrin.** By A. PRIBRAM. (*Prager. med. Wochenschrift*, 1884, N. 40—47).

In the great majority of cases which were treated with Antipyrin the desired antipyretic effect did not fail to appear. Only in one case of suppurative pericarditis and pleuritis the septic fever was not materially lessened by Antipyrin, although up to two drachms had been given during 48 hours. Antipyrin is slowly eliminated from the body, a circumstance which partly explains why such a lasting effect is produced. A few hours after administration of the first dose Antipyrin appears in the urine, in which it may be recognised by its reaction with perchloride of iron. Soon after, the reaction increases in intensity, reaches its height and decreases, but remains present for more than 12 hours.

With regard to the dose the author states, that with 15 grain doses (3 Tabloids) repeated every hour, the results were as good and the abatement of temperature as efficient as with Filchne's method of giving 30+30+15 grains (6+6+3 Tabloids).

The author fully confirms other statements with regard to the alteration in the frequency of the pulse and in arterial tension.

Of secondary effects the author saw vomiting and abundant sweating, but never alarming symptoms; sometimes the patients

complained of a feeling of weight on the stomach. A serious but not fatal collapse set in in one case of tuberculosis, with high fever and great prostration. The total dose in this case amounted to 60 grains (12 Tabloids).

The author saw five cases of Antipyrin rash, which in four cases had the appearance of measles; in one case it was similar to urticaria.

The author does not hesitate to state that Antipyrin in the treatment of typhoid fever is superior to Quinine, as it has no depressing influence on the functions of the brain.

A specific action materially altering the course and duration of the disease was not observed. Engorgement of the spleen was unaffected by the drug.

In tubercular disease of the lungs the temperature was often kept at moderate height by small doses of the drug, whereby the general condition of the patients was much improved, and the otherwise rapid general decay somewhat retarded, but the progress of pathological changes and the general course of the disease was not altered. Sometimes a marked increase of the bodily weight was recorded after Antipyrin. It however soon decreased again when the remedy was discontinued, and the febrile temperature re-established itself.

**From the Internal Clinic of Prof. von Dusch in Heidelberg.**—On the action of ANTIPYRIN in Children and Adults. By A. GEIER. (*Deutsche med. Wochenschr.* 1884, N. 95).

The author reports on 11 cases of febrile diseases treated with Antipyrin, 5 of them concerned children of 1 to 13 years of age.

With only one exception the temperature was reduced by Antipyrin most energetically. Children sometimes vomited after having taken the drug. Phthisical patients perspired much in consequence of the medication. Once an eruption was seen, which however did not cause any discomfort.

The author is of opinion that Antipyrin will soon replace Quinine in many of the different classes of fever. It is entitled to such a dominant position by its constant and prompt antipyretic action and by the rarity of disagreeable secondary effects.



**On the Value of Antipyrin as an Antipyretic.—**

By A. v. HOFER (*Wiener med. Wochenschrift*, N. 47).

The author reports on his constantly successful results with the Antipyrin treatment, even in one case of chronic pyæmia and another of endocarditis, Antipyrin fulfilled all expectations (cf. Pribram).

Hectic fever and hectic perspiration of consumptive patients were simultaneously moderated by the combined action of Antipyrin and Atropine.

Vomiting was seen several times, especially after large doses. He therefore recommends 15-grain doses (3 Tabloids) every three hours (5 to 10 grains—1 to 2 Tabloids—for children). Vomiting is thereby prevented.

If the remedy is given per rectum, larger doses—1 drachm and more—are necessary. The subcutaneous method did not satisfy Hofer.

**Recherches thérapeutiques sur un nouvel antipyrétique, l'antipyrine.** Par HENRI HUCHARD, Médecin de l'hôpital Bichat in Paris. (*Union médicale*, 1884, N. 169).

Huchard was the first French physician who used Antipyrin. He gave it in many different fevers, and from a very large experience of the use of the drug he draws the following conclusions: Antipyrin is a reliable and powerful remedy for reducing the temperature in nearly all the febrile diseases. Not only temperature, but also other febrile symptoms are favourably influenced, such as increase of frequency of pulse and respiration, dryness of the mucous membrane, etc. A direct action on respiration and circulation is not traceable.

Antipyrin is a purely antipyretic remedy. It has no specific action. In cases of intermittent fever it does not prevent the recurrence of attacks.

Disturbances caused by Antipyrin are slight, if occurring at all. They consist of slight perspiration, occasional drowsiness and vomiting, rarely of scarlatina or measles-like eruptions. Inclination for collapse and delirium, as sometimes observed after quinine or salicylic acid have been given, have never occurred. Number-

less observations prove that Antipyrin is the most powerful and the only remedy known for reducing the fever of consumptive patients. Thirty grains (6 Tabloids) given towards the evening reduce the temperature in the course of  $1\frac{1}{2}$ —2 hours to its normal level; sometimes the dose has to be repeated 1 or 2 hours afterwards.

The antipyretic effect usually lasts for 6—9 hours. Subsequent rising of temperature is gradual, and never accompanied by rigor.

Antipyrin is eliminated by the urine in the course of  $1\frac{1}{2}$ —2 days.

**On the action of Antipyrin.** By Dr. NEUFELD, in Sasnowice. (*Gazeta lekarska*, 40/84).

The author had the opportunity to try Antipyrin during an epidemic of typhoid fever in the village of Dzbowa Gôra. He treated 22 cases with the new remedy. The following are his conclusions:—Antipyrin is a reliable febrifuge in all cases of fever. It is comparatively free from unpleasant after-effects, occasional vomiting being the only drawback to which the patient may be subject.

Single doses for adults: 30 grains (6 Tabloids); daily dose, 90 grains (6+6+6 Tabloids). The reduction of temperature sets in one hour after Antipyrin has been taken; even sooner in the case of subcutaneous application. Temperatures of  $94^{\circ}$  have been observed after a full dose (90 grains). If the depression is so great, a second dose ought not to be given unless the temperature has risen again to  $103^{\circ}$ .

In malaria the temperature is reduced by Antipyrin, just as it is in all other fevers. But a specific influence on the morbid process itself is not observed.

**Antipyrin in Phthisis.** By Dr. MEISSEN, Physician to the Sanatorium of Falkenstein, i. T. (*Deutsche med. Wochenschrift*, 1884, N. 51).

The author speaks most highly of the prompt and constant action of Antipyrin in cases of typhoid. It compares most favourably with quinine and salicylic acid, both of which cause discomfort in the head and stomach, and hardly affect the tempera-

ture at all. The phthisical patients felt better altogether after they had taken Antipyrin ; even the appetite often improved.

Disagreeable after-effects, such as humming in the ears, dizziness in the head, vertigo, vomiting, loss of appetite, which frequently appear whenever quinine or salicylic acid is given to consumptive patients, did not occur if a judicious use of Antipyrin was made. When Antipyrin was taken for a prolonged time, a certain adaptation of the body to the new drug seemed to take place.

Reduction of temperature was always accompanied by perspiration. Too abundant sweating was checked by simultaneous administration of agaricin (first recommended by Norden). Rising of temperature was gradual and slow ; never with rigors.

A rash, apparently from the medication, appeared in 10 per cent. of the cases. It was erythema- or urticaria-like, did not do any harm, and disappeared soon when the remedy was discontinued.

The author recommends to give smaller doses in phthisis than in other febrile diseases. He found it most convenient to reduce the fever to about  $100^{\circ}$ , for which purpose repeated doses of gr. 10—15 (2 to 3 Tabloids) proved sufficient.

**Notes sur l'Antipyrin.**—By RAPIN (*Rév. méd. de la Suisse romande*, 1884, pag. 404).

Antipyretic effect was produced even in cases where quinine and cold baths failed to reduce the temperature. There was only one exception. In one case of ulcerative endocarditis no effect was obtained with Antipyrin.

The subcutaneous method being too painful was given up.

**From the Royal Hungarian Hospital at Pressburg.**  
—On new remedies and how to prescribe them, communication made by Pávay. (*Pester med. chir. Presse*, 1885, N. 2—4.)

The author used Antipyrin very extensively. He gave it as mixture, powder, enema, or subcutaneous injection. His doses somewhat differ from those of other investigators. He gave small doses of 10 grains (2 Tabloids), but repeated this dose every four hours. If the temperature was at  $102^{\circ}$ , the dose was given three times ; if at  $103^{\circ}$ , four times ; if at  $104^{\circ}$  or  $105^{\circ}$ , six times. By

this method the temperature was kept at  $98^{\circ}$  or  $100^{\circ}$  at least for about one or two hours each day. Nausea, vomiting, humming of the ears, did not occur if the drug was given for a short time only. If continued for six to eight weeks, loss of appetite, oppression, nausea was the consequence. Caution is necessary in cases of weakened heart.

Subcutaneous injection had a very rapid effect. Three injections of 15 grains (3 Tabloids) each, applied at half-an-hour's interval, reduced temperatures (in typhoid fever and phthisis) of  $104^{\circ}$  to  $100^{\circ}$ .

The subcutaneous method was devoid of any disagreeable secondary symptoms.

In cases where the mucous coat of the stomach was affected, and where the subcutaneous method was difficult in consequence of advanced emaciation, Antipyrin was given per rectum (dose 45 grains) with perfect success.

The longest period during which a patient was kept apyretic by the use of Antipyrin was 12—16, the shortest two to six hours.

**From the Civil Hospital of Nürnberg.** — On ANTI-PYRIN, by MAX REIHLEN (*Inaugur. Dissert. Stuttgart*, 1885).

The author observed the effect of Antipyrin in not less than 56 cases. In the great majority of those cases a very powerful and decided effect of the drug was obtained. If any retardation was recorded, a distinct cause (gastric catarrh, for instance) preventing the rapid absorption of the drug, could be found. Degree, duration, rapidity of falling and rising of temperature depend, if we exclude the question of dose, upon the following factors:—

1. Age, sex, constitution of the patient. Persons of 16—21 years are more affected than older patients. The effect is greatest with people who have not been much pulled down by former illness.

2. Kind and stage of the disease. Tuberculosis is easily influenced. Acute infectious diseases require stronger doses. Erysipelas is the most obstinate. Pneumonia, typhoid, gangrene of the lungs, follow in the order of their enumeration.

The importance of the stage of the disease is most evident in

typhoid fever, where with the beginning of the third week the fever offers less resistance every day.

3. Period of administration : previous to or simultaneous with other antipyretic measures. If the effect of Antipyrin coincides with a spontaneous abatement of temperature, a subnormal falling and threatening collapse takes place. Antipyrin, combined with other antipyretic measures (cold baths), produced very powerful effects.

4. Division of the total dose : small fractions often repeated does not act well. The effect differs in cases where the total dose is given within 2 hours from those where 3 to 4 hours is the period chosen. 45+30 grains (9+6 Tabloids) given during 2 hours reduced generally more than 30+30+15 grains given during 3 hours.

To give Antipyrin by the mouth is the simplest and best way of administration.

Dr. Reihlen, a very judicious and careful observer, noticed the following secondary effects :—

Rigor in one case ; slight shivering, whilst the temperature went up again, in several cases ; more or less abundant perspiration, which however never discomforted the patients, was noticed in nearly all cases ; it coincided with the fall in temperature. Vomiting was rare. The frequency of pulse mostly diminished simultaneously with the temperature ; sometimes it was slightly postponed. In four cases of typhoid fever a macular eruption was observed (Antipyrin rash), in one case a very distinct miliaria alba.

The author concludes with the remark that the antipyretic effect lasts for a much longer period than with any other febrifuge remedy. Its principal advantages, however, consist in the absolute certainty of the effect, in the absence of disagreeable secondary effects, and in the perfect harmlessness of the remedy, if the slightest care is observed during its action.

**From the Internal Department of the Civil Hospital at Dresden,** under the direction of Privy Councillor Dr. Fiedler.—On ANTIPYRIN. By DR. PUSINELLI (*Deutsche med. Wochenschrift*, 1885, N. 10).



The author observed the effect of Antipyrin in 100 different cases (42 of which were typhoid fever).

He confirms the statements with regard to the absolutely certain and constant action of the drug. Degree and duration of the effect depend upon the malady, upon age, sex, and constitution of the patient. The author recommends to administer a test dose of 10—15 grains (2 to 3 Tabloids) before beginning the proper treatment with Antipyrin. This is done for the purpose of finding out the individual reaction against the drug. Larger doses (15 and 30 grains) ought not to be repeated every hour unless there is provision for exact measurement being taken every hour.

In high fever, Antipyrin favourably influences the functions of the brain, and is, therefore, in this respect, much superior to quinine. Other advantages are its ready solubility and absorption, and its absolutely certain action, even in very high fever. Kairin and hydrochinon are much inferior to Antipyrin, as they are apt to cause collapse and rigor, and as their temperature-reducing properties are not so powerful as is the case with Antipyrin.

**From the Internal Clinic of Prof. Rossbach in Jena.**—Some remarks on the action of ANTIPYRIN, by Dr. GOETZE, First Assistant (*Berlin. klin. Wochenschrift*, 1885, N. 10).

Goetze used Antipyrin in all kinds of different fevers with great success, and without discomfort to the patient, two cases of collapse excepted. For obviating the latter, the author recommends to first test the patient's susceptibility by small doses. Antipyrin rash appeared in five cases.

**From the Internal Clinic of Prof. Eichhorst in Zürich.**—Observations on the febrifuge action of Antipyrin and Thallin, by Miss Dr. Sara WELT (*Dtschs. Archiv. für kl. Medicin*, 1885).

From July, 1884, to April, 1885, the number of patients treated with Antipyrin at the Clinic of Zürich amounted to 122. Not less than 1,134 single doses had been prescribed. The remedy was mostly administered in the form of an enema, containing a sufficiently large dose. The susceptibility of the patient had previously been tested by small doses. In cases of pneumonia and erysipelas

it was found necessary to increase the dose in proportion to the progress which the morbid changes had made.

Antipyrin rash was observed in 10.6 per cent. of the cases. All cases with rash, except one, were typhoid fever.

The author obtained excellent results with Antipyrin in the treatment of the hectic fever of consumption.

Bielschowsky's presumption, that Antipyrin favours the occurrence of hæmorrhage from the lungs, is not confirmed by Welt.

Disagreeable and threatening symptoms deriving from the medication were never observed.

The author concludes with a comparison between the action of Antipyrin and of Thallin. After 114 single doses of Thallin, rigors were observed 17 times=12%; after 1,134 doses of Antipyrin 6 times=0.5%. Vomiting occurred in 7.1% of the Thallin cases; in 13.5% of the Antipyrin cases. Besides this, Thallin several times caused diarrhœa; in one case albuminuria, which disappeared as soon as Thallin was discontinued.

With regard to the duration of the effect Antipyrin is far superior to Thallin.

Thallin, like Antipyrin, has no specific influence on the course of the disease.

**Antipyrin in Phthisis.**—By Dr. P. KAATZER, physician to the Bath of Rehburg (*Deutsche med. Wochenschrift*, 1885, N. 17).

Quinine and salicylic acid have not secured themselves a permanent place in the treatment of phthisis. Their action is uncertain, and often accompanied by undesirable symptoms. Antipyrin, which is free from the latter, and which acts promptly, represents therefore a decided advance in the treatment of consumption. Kaatzer gave it according to Filchne's method; the usual evening exacerbations of temperature were greatly moderated by even small doses of the remedy; high continuous fever was transformed into the remittent type. Sleep, appetite and the general condition of the patient showed great improvement after this treatment.

It is true that abundant perspiration sometimes occurred, but it never discomfited the patient. It was relieved by changing the dress, rubbing of the body with a towel. It never was so abundant

as after administration of kairin or of salicylic acid. Antipyrin rash was observed twice.

**From the Ducal Hospital at Brunswick.**—Treatment of Typhoid Fever with ANTIPYRIN. By DR. RICHARD SCHULZ, Director of the Medical Department (*Deutsche med. Wochenschrift*, 1885, N. 20).

The effect of Antipyrin in typhoid fever was studied by the author in 17 cases. Filehne's plan was followed; 30+30+15 grains—6+6+3 Tabloids (with one hour's interval) brought the fever, which usually amounted to at least 104°, down to the normal temperature. In one case of typhoid, combined with pneumonia, it required 120 grains (four times 30 grains—6+6+6+6 Tabloids 5 gr.), by which dose the temperature was reduced from 106° to 98°4. In two cases subnormal temperatures were observed, 90° and 94.8° after 60 and after 45 grains respectively.

Abatement of temperature, with perspiration and subsequent rising, sometimes with slight shivering, were the only symptoms caused by Antipyrin. Vomiting did not occur. Digestion and splenic enlargement were not altered by the medication.

The author recommends preparatory trial with a small dose, to find out the patient's susceptibility.

**From the Civil Hospital Moabit in Berlin.**—On Antipyretic Remedies. Paper read at the Medical Society on the 21st of April, by DR. PAUL GUTTMANN, Medical Director of the Moabit Hospital (*Berlin klin. Wochenschrift*, N. 24 and 25).

The author first deals with the question of the value of antipyretic measures in general and antipyretic remedies in particular. He then compares the action of the different ancient and modern antipyretics. With regard to Antipyrin, he fully confirms his former statements and the experience of many others. Guttman watched the Antipyrin treatment in not less than 297 different cases. his conclusions are therefore of great value. Even in obstinate cases the fever was almost uniformly lessened, and only in very exceptional cases was no effect seen. In half of the cases more or less profuse perspiration took place whilst the temperature went down; rigors never set in.



Antipyrin rash, mostly resembling measles, was observed in six cases of different febrile disorders.

Acute rheumatic fever is the only disease which is directly influenced and shortened in its course by Antipyrin. Even in chronic rheumatic arthritis a favourable effect was sometimes obtained by Antipyrin.

Thallin is not so reliable as Antipyrin, and the rise following abatement of the temperature was accompanied by rigors.

**From the Hôpital Bichat at Paris.**—*Etudes thérapeutiques sur L'ANTIPYRIN*, par HENRI HUCHARD, Physician to the Hôpital Bichat (*Extr. des Bull. de la société de thérapeutique, Janvier et Février, 1885*).

Further experience with Antipyrin fully confirms what the author has stated in a previous publication. The most striking results were obtained in cases of typhoid fever. Antipyrin combines all the necessary qualities for an excellent febrifuge in diseases of children. It is very soluble, possesses hardly any taste, and is perfectly harmless.

Antipyrin may either be given by the mouth or per rectum, or by the subcutaneous method. The first way is the most convenient. Its action is uncertain if it is applied to the rectum in the shape of suppositories.

After 15—20 grains (3—4 Tabloids), profuse perspiration frequently sets in. To avoid the latter, Huchard gave smaller doses (8—12 grains), repeated every one-and-a-half or two hours. His doses are altogether smaller than those used by the German authors.

**Osservazioni pratiche sull' azione dell' Antipyrin.**—By MONTI, of Bologna (*Bull. della scienze med. di Bol.*, 1885. *Scr. vii.*, Vol. V.).

Monti's observations fully confirm the statements with regard to the powerful action of Antipyrin. The promptitude with which Antipyrin is eliminated through the urine varies. If given per os, the reaction with perchloride of iron is stronger in health than in the febrile state. The reverse is the case if Antipyrin is given per rectum. In cases where the subcutaneous method was preferred,

the reaction was very slight. Healthy people even had in this case no reaction at all.

**Will. Draper.** *Antipyrin and its effects* (*Boston Med. and Surg. Journal*, 1885, April 21, p. 395).

**Schattuck, George.**—The results of the use of Antipyrin in the Boston City Hospital.

Both authors report very favourably on their trials with Antipyrin. They consider it of especial value in the treatment of typhoid fever. Pulse frequency decreased to an extent corresponding to the reduction of temperature. In two cases antipyretic action was obtained where the cold bath system had failed.

**Étude clinique sur la valeur de l'Antipyrin spécialement appliquée à la thérapeutique infantile.**—By LAURE (Lyon) (*Rév. mensuelle des maladies de l'enfance*. Février, 1886).

The author prescribed Antipyrin every three hours in doses of 2, 3, 5, or 10 grains, according to the age of the patient. He thinks that Antipyrin is indicated in all cases where the fever amounts to 102° and upwards. Profuse perspiration is pretty frequent even after small doses, and its occurrence often prohibits a prolonged use of the drug. The author records the beneficial influence of Antipyrin in typhoid fever, pneumonia, acute rheumatic fever and scarlet fever; nowhere was its success so well marked as in tubercular diseases of children with high fever. Not only was the fever lessened, but great relief afforded to the patient's general condition.

**Observations on Antipyrin in infectious diseases of Children.** By Dr. BUNGEROTH (*Char. Annal.*, Bd. XI., p. 599, 1886.)

Cautious administration of Antipyrin acts very beneficially. The dose has to be varied according to age, previous state of health, and intensity of fever and morbid process. Doses of 5—7 grains (1—1½ Tabloids) were often found sufficient, even with elder children, for completely reducing the temperature.

In typhoid fever Antipyrin had a favourable influence, not only on the temperature, but on the functions of the brain as well; diarrhoea was not infrequently improved and the secretion of urine

increased. The perspiration conjointly occurring with the reduction of temperature was mostly an agreeable event to the patient.

Scarlet fever often offered considerable resistance to the action of Antipyrin, whilst cases of pneumonia did very well on it.

In diphtheria signs of impaired action of the heart were observed after Antipyrin; the author therefore cannot recommend Antipyrin for diphtheria.

**De l'action antipyrétique et antirhumatismale de l'antifébrin.**—Par le Dr. P. SNYERS (*Extr. des annales de la société méd. chir. de Liège, Déc. 1886*).

The author draws a parallel between the antipyretic action of Antipyrin and Antifebrin. He is in favour of Antipyrin, because it has a longer lasting effect than Antifebrin.

**Communications from the Municipal Hospital at Wiesbaden on an Epidemic of Typhoid Fever,** which occurred in the summer of 1885.—By EMIL KNEBEL (*Inaug. Dissert. München, 1886*).

The treatment consisted of baths and the administration of calomel and Antipyrin. The patients took 30 grains (6 Tabloids) of Antipyrin (15—3 Tabloids—in cases of children), if at 3 p.m. the temperature was above 104°. Two hours afterwards the temperature was taken again. If it amounted to more than 101°, another 30 grains (6 Tabloids); if to less, another 15 grains were given; if to 100° or less, no second dose was given. The antipyretic effect was mostly well pronounced, and was even noticeable the following day. Rigors, collapse, nausea very seldom occurred. Antipyrin rash appeared several times.

**Typhus treated with Antipyrin.**—By Dr. HERMANN HAAS (*Prager med. Wochenschr., 1886, N. 46*).

The author reports on his experience with the Antipyrin treatment of typhus, and compares the results with those obtained by quinine treatment. Both remedies were given in the same quantities, three grains every two hours. Only cases where the diagnosis was absolutely certain were chosen. It was evident that quinine had no effect, whilst with Antipyrin the constant fever

was lessened, the temperature being 2—5 degrees lower after Antipyrin had been given for two or three days. Antipyrin had no specific influence on the disease itself, although its course seemed somewhat milder and shorter under the Antipyrin treatment. The preparation never caused any unpleasant symptoms.

**Notes sur l'Antifebrin.**—By Dr. LOUIS SECRETAN (*Rév. méd. de la Suisse romande VII., I. 1887*).

The result of Secretan's investigations indicates that Antifebrin, though a reliable and powerful antipyretic, cannot compete with Antipyrin with regard to the duration of the effect. Also in cases of rheumatic fever it did not seem to act so well as Antipyrin.

**On Antipyrin in children's practice** (scarlet fever and bronchitis).—By Dr. JUL. FRIEDLANDER, Pluvigiany Gouv. Kowno, Russia (*Ther. Monatshefte, 1887, Heft 8*).

The author obtained excellent results with Antipyrin in cases of scarlet fever and bronchitis. The former disease was not materially altered in its course by the remedy, but the little patients felt much better with it. They were less fidgety, and took nourishment more willingly.

In acute bronchitis Antipyrin acted even better. The course of the disease (especially if high fever was present) was shortened and its character was mitigated. Whilst formerly the mortality amounted to 50 per cent., it was only 10 per cent. under the new treatment. Antipyrin may therefore be said to be a most valuable remedy for the diseases mentioned above. In cases where the child's hygienic surroundings were good, it nearly always effected a cure.

The author prescribed 10—15 grain doses (2 to 3 Tabloids) of Antipyrin; 10 grains (2 Tabloids) given to children below two years produced an effect lasting for 20 hours; 15 grains (3 Tabloids) given to older children (up to five years) kept the temperature down for 12—15 hours. Besides Antipyrin, wine and caffèine were sometimes given. The cough was relieved after three to five days; the children became more lively and began to play again. The cure seemed to be effected more rapidly with children who showed profuse perspiration after Antipyrin.

**On the treatment of Hectic Fever.**—By Prof. ALFRED PRIBRAM, Director of the I. Med. clinic at Prague (*Prager med. Wochenschrift*, 1887, N. 36).

The author thinks that full doses of Antipyrin are sometimes accompanied by disagreeable secondary effects—vomiting, inclination to collapse, hæmorrhage. He further observed that the subsequent rising of the temperature is often proportionate to the artificial reduction. He therefore proposes to use small doses of Antipyrin for combating hectic fever. His experiments showed that doses of 10 grains (2 Tabloids) and less are able to reduce the febrile temperature of phthisical patients to the extent of at least one to two degrees.

He proceeded in such a way that he first obtained a curve of the regular fluctuations of the patient's temperature. He then gave one ounce of one per cent. Antipyrin solution half-an-hour before the usual rising of temperature was to be expected. Every hour another half-ounce of the solution is given until the temperature is reduced to 38°. If the concentration of 1 per cent. should not prove sufficiently strong, a 1½ or 2 per cent. solution is given instead, and this treatment continued for five to six days. After this time the usual quantity is a little diminished, and after another few days a second portion of the dose is given up, and so on. Even if after a few days the temperature never exceeds 100°, it is advisable to give a single dose of the solution half-an-hour before the former rise of temperature.

Antipyrin is superior to all other antipyretics, because it is most reliable in its action, and because it has least secondary effects.

**Mas sobre la Antipyrina, por Suñer.** (*El Siglo Medico* XXXV., 1888, p. 497).

In a case of chronic cystitis and consecutive nephritis, the secretion of urine was scanty. It was therefore desirable to stimulate the secretory functions of the skin. For this purpose Antipyrin was given, which favourably influenced the quality of the pulse, and succeeded in greatly improving the general conditions of the patient.



**Clinical experience of Antipyrin.** By THOM. OLIVER, M.D., Physician to the Royal Infirmary at Durham. (*Brit. Med. Journal*, May 5, 1888).

The author declares that Antipyrin is a drug which has a wonderful power in reducing high temperature, and that quickly. In some cases of typhoid fever he has known it to reduce the temperature from  $106^{\circ}$  to  $101^{\circ}$  within two hours. It gives the same result as cold baths, without exposing the patient to the dangers of the latter. After the first two doses of 15 grains (3 Tabloids), he began to use only small doses of 7 to 10 grains ( $1\frac{1}{2}$  to 2 Tabloids).

In one case of chorea, where arsenic, bromides, chloral, etc., had failed, Antipyrin given in 7 grain doses effected a perfect cure.

In a case of locomotor ataxy, the burning sensations on the soles of the feet disappeared after Antipyrin.

## II.—ANTIPYRIN AS AN ANTI-RHEUMATIC.

**Antipyrin in cases of Rheumatic Fever.** By Dr. LENHARTZ, BERLIN, (*Verhandl. des Vereins für inn Med.*, 1884).

The author reports on 24 mostly serious cases of rheumatic fever treated with Antipyrin, each case having previously been treated with salicylate of soda. The result was that Antipyrin reduced and sometimes completely annihilated the fever, removing all pains and swelling of the joints. In a few cases where salicylate of soda had failed to have any effect, Antipyrin showed favourable results. No ill-effects were observed. Humming of the ears and vertigo, which were regularly seen after salicylate (in one case even cerebral symptoms), never occurred after Antipyrin. The drug could not prevent recurrence of the disease.

**Therapeutic experiments** by STERN, of PEST (*Pester Med. Presse*, 1885, N. 15). Stern fully confirms Lenhartz's statements with regard to the very favourable action of Antipyrin in rheumatic fever. The drug lessens the fever, and has a specific effect on the inflammatory lesions of the joints.

**Note sur l'Antipyrin.** By CLÉMENT (*Lyon Med.*, 1885, No. 25, page 265).

Antipyrin in the treatment of rheumatic fever is a successful rival of salicylate of soda. It has exactly the same effect as the latter, but without its disadvantages.

**From the Civil Hospital Moabit in Berlin.**—ANTI-PYRIN in cases of acute rheumatic affections of the joints, by Dr. H. NEUMANN, Assistant Physician to the Hospital (*Berlin klin. Wochenschrift*, N. 37).

After having briefly alluded to the growing Antipyrin literature the author reports on his experience with 17 cases of rheumatic fever treated with Antipyrin, partly in conjunction with salicylate of soda. Neumann confirms Demme's opinion, that the therapeutic effect obtained with Antipyrin in cases of rheumatic fever is identical with that of salicylate of soda. Prompt alleviation of articular tenderness, and more or less rapid disappearance of the swellings of the joints are prominent effects; like salicylate it does not protect against cardiac complications, nor does it prevent recurrence of the disease. Cases where both anti-rheumatics failed to have any effect were very rare; in a few cases the one acted well, while the other failed. Antipyrin has the advantage over salicylic acid of being less poisonous than the latter.

The author backs his assertion by a number of carefully recorded patients' histories. He finally states that even chronic rheumatism and rheumatic neuralgia are sometimes favourably influenced by Antipyrin.

**On the effect of Antipyrin in Rheumatic Arthritis.**—By Dr. GOLEBIEWSKY, of Berlin (*Berlin klin. Wochenschrift*, 1886, N. 28).

The author reports on his experience with 70 cases of rheumatic fever treated with Antipyrin. He considers Antipyrin a specific in this disease, just as is salicylic acid. Only in one case of rheumatic affection of both shoulder joints Antipyrin remained inefficacious, but such failures were pretty frequent with salicylate.

Generally the effect was very prompt. The complete disappearance of articular swelling corresponded to the low state of the

temperature. The average duration of the illness until all inflammatory signs had subsided was three to four days.

The effect was most certain with large doses, but even daily doses of one drachm removed all traces of articular swelling in the course of four to five days. Small doses were indicated with patients of weak constitution.

Antipyrin was efficacious in acute as well as in chronic cases; endocarditic symptoms were hardly influenced at all; complete rest in bed, and ice-bag did more good in such cases. Relapses were not prevented by Antipyrin.

Collapse, even with daily doses of 150 grains, never occurred; slight rashes were observed twice; they disappeared without special treatment and without interruption of the Antipyrin treatment. The occurrence of sweating was very irregular; vomiting was seen pretty frequently, but it several times was the consequence of an inappropriate method of administration.

**On Antipyrin Treatment of Acute Rheumatic Fever.** Paper read before the Medical Society on the 18th October, 1886. By Professor A. FRÄNKEL (*Deutsche med. Wochenschrift*, 1886, N. 43 and 44).

Fränkel treated 34 cases of rheumatic fever (13 light and 21 severe cases) with Antipyrin; and, taking at the same time into consideration the experience of other authors, he draws the following conclusions.

I. Antipyrin has to be considered a specific against rheumatic fever. A great number of the cases which were under his care, even if they had already lasted for a considerable time, were promptly cured by Antipyrin.

II. Advantages of the Antipyrin treatment over other treatments of acute rheumatic fever are:—easy and convenient administration, and rarity of unpleasant after-effects. (The author observed once vomiting, twice rash, never collapse.) The question whether Antipyrin is able to prevent or lessen the occurrence of inflammatory changes of the thoracic organs, in particular the heart, cannot yet be decided.

III. Antipyrin cannot entirely substitute other specifics against



acute rheumatic fever, especially salicylic acid, since there are cases which resist Antipyrin, whilst they do well on salicylic acid. The reverse may happen as well. Furthermore, there are cases which under Antipyrin treatment easily recur, requiring the continued use of the drug for several weeks, and requiring sometimes the administration of other anti-rheumatics.

IV. A contra-indication for the use of Antipyrin in rheumatic fevers does not exist. Its discontinuance may be necessary if absolute disinclination against the remedy, or severe medicinal rash should appear as a consequence of the drug.

**De l'Antipyrin dans le Rheumatism Articulaire aigue avec complications diverses.** Par le Docteur E. CLÉMENT. (*Lyon Med.* XVII., 35, p. 567).

The author thinks that Antipyrin is a specific in acute and sub-acute rheumatic fever, and will have a brilliant future, as it is much superior to salicylic acid. In many cases where the latter failed a cure was effected by Antipyrin, for which there is no contra-indication, not even advanced heart or kidney disease. In chronic rheumatism, Antipyrin does not do much good. The author further states that in two cases of gout, Antipyrin was marvellously successful—swelling and pains disappeared within a few hours.

### III.—ANTIPYRIN AS AN ANODYNE.

**From the Hospital Bichat in Paris.**—Etudes thérapeutiques sur l'Antipyrin par Henri Huchard, physician to the Hospital, Paris, 1885 (*Bulletin de la Société de thérapeutique.* Janvier and Fevrier, 1885.)

In a case of exophthalmic goitre the cardiac paroxysms were suppressed by Antipyrin given in small doses, also the enlargement of the thyroid gland was considerably reduced.

**Sur l'Antipyrin considérée comme médicament nervin,** par P. LÉPINE. (*Lyon Méd.* LII. 33, p. 501, 1886.)

The author concludes from his observations that Antipyrin, when there is no fever, causes a kind of cerebral agitation. Pains

are allayed by this "Ivresse Antipyrrique;" a similar state is caused by morphia and salicylic acid. Cases of locomotor ataxy with lancinating pains were much benefited by Antipyrin. Doses of 150 grains *pro die* entirely removed all pain, whilst the atactic symptoms temporarily increased, and the patients complained of sleeplessness.

Antipyrin is therefore an anodyne of primary importance. It will be a matter of further investigations to limit the indications for this new drug.

**Antipyrin as an analgesic in Head-ache.**—By T. BLAKE-WHITE (*New York Med. Rec.* XXX. 2, p. 293, 1886.)

The author tried Antipyrin in different cases of head-ache with decided success. Especially in the migraine form, given as soon as the pain sets in, it proved to be excellent.

**Antipyrin in Hemicrania.**—By Dr. E. UNGAR, Lecturer at the University of Bonn (*Centralbl. f. klin. Med.* VII., N. 45, 1886.)

The action of salicylic acid and Antipyrin so much resemble each other that the author was induced to try Antipyrin in hemicrania, in which disease salicylic acid often cuts short the attacks. The effect was very good. Antipyrin given at the onset or during the period of precursory symptoms in most of the cases prevents the occurrence of a typical attack, or at the least mitigates its course. This very satisfactory success was even obtained, in some instances, where all previous medication had failed.

Antipyrin, of course, is no panacea; in some cases the expected effect entirely failed to appear, in others the effect was but slight.

If Antipyrin acted at all, a single dose of 15 grains (3 Tabloids) was usually sufficient. Within an hour the pain was greatly diminished. Sometimes another dose of 15 grains (3 Tabloids) became necessary.

The drug caused neither discomfort nor any ill-effects whatever.

A satisfactory explanation for the action of Antipyrin in hemicrania has not yet been given and is not likely to be soon found out, as the etiology of the complaint itself is still very obscure.

**Antipyrin a Remedy for Sleeplessness.**—By Dr. W. BRAYTON-CAREY (*The Med. Record*, XXXII., N. 22, 1887).

A lady, who had had a very severe confinement, during which she was greatly weakened by hæmorrhage, could not obtain any sleep with the aid of the ordinary narcotics. After she had passed five consecutive nights without sleep, the author ordered six grains of Antipyrin, together with two grains of antifebrin. The patient after this had six hours refreshing sleep. The same mixture was repeated for four evenings, each time with the desired effect.

**Antipyrin as an Anti-neuralgic.**—By Dr. MARTIUS, of Ansbach (*Munich med. Wochenschrift*, 1887, N. 2).

The author, following Ungar's plan, used Antipyrin with marked success in all kinds of neuralgia. Shooting pains and cramps of diabetic patients were much alleviated by it.

Ten grains (2 Tabloids) given in warm water, on an empty stomach, was usually sufficient for obtaining the desired effect. The dose was repeated if after 40 minutes no effect was visible.

**A case of Chorea minor treated with Antipyrin.**—By Dr. WOLLNER (*Munich med. Wochenschrift*, 1887, N. 5).

The author reports on a case of chorea in a girl aged 16 years, who had previously had a slight attack of rheumatic fever. Bromide of potassium, propylamine and salicylic acid had been given, one after the other, but to no avail. Antipyrin (15 grains—3 Tabloids—three times a day) instantly influenced the disease, and within 12 days the patient was cured of chorea.

**De l'Antipyrin contre la douleur.**—Note de M. Germain Sée, physician to the Hôtel Dieu, Paris (*Comptes rendus t. CIV.*, N. 16, p. 1085.)

Germain Sée, like all other clinical teachers, first tried Antipyrin solely to reduce fever. But he found that other prominent properties of the new drug are of much greater importance than its antipyretic action. Rheumatic, neuralgic, and other painful affections form a vast field for the use of Antipyrin.

In 15 cases of febrile rheumatism, where all the usual remedies had been tried without benefit, pains and swellings disappeared in a few days when Antipyrin was administered. When the latter

was continued in small doses after all pain had gone, no recurrence of the affection was observed. A similarly successful treatment was obtained in cases of acute and chronic gout.

The author especially points out how calming the effect of Antipyrin is in cases of nervous disorders. He gives the records of 14 different cases of painful affections of the head, which were all cured by Antipyrin in a very short time. The series comprised four cases of facial neuralgia, five cases of migraine of old standing; the others were different cases of cephalalgia, some of which were associated with rapid growth.

A second series included 18 cases of nerve and muscular pains of persons afflicted with diabetes, locomotor ataxy, herpes zoster, and indefinite pains of cachectic patients and people of general nervous disposition. All those cases were favourably influenced by Antipyrin, as were also pains frequently associated with diseases of the heart, the cardiac and aortic arteries.

The minimum dose, giving a favourable effect, was 30 grains (6 Tabloids), the maximum 90 grains (divided into doses of 15 grains, 3 Tabloids each, given every one to three hours). The medication never caused any undesirable effect on the action of the heart, respiration, or secretion of the kidneys. The only unpleasant after-effect of large doses consisted of a scarlatina-like eruption. Antifebrin, which possesses anodyne properties similar to Antipyrin, owing to aniline impurities, often causes serious alterations of the blood. Antipyrin is therefore much preferable, as it has at least the same effect, and does not expose the patient to any danger.

**L'Antipyrin en Injections sous-cutanées substituées a la Morphine.** Notes de M. GERMAIN SÉE. (*Comptes rendus t. CV., N. 2., p. 103*).

With the view to accumulate and accelerate the action of Antipyrin, and at the same time to relieve the stomach, the author applied Antipyrin sub-cutaneously (50 per cent. aqueous solution). By this method a considerable diminution of all kinds of pains was effected. The patient was not exposed to any danger or discomfort, such as is frequently observed after morphia. Whilst the latter acts purely symptomatically, Antipyrin often directly

influences the source of pain. To prove this, the author reports on numerous cases of different painful affections which he treated in this way—articular rheumatism, chronic gout, one case of particularly distressing acute gout, were treated by internal administration of Antipyrin, combined with a few sub-cutaneous injections, which acted marvellously. Facial neuralgia, lumbago, and migraine, were cured nearly instantaneously. Atactic gait was suppressed by daily injections of Antipyrin, in conjunction with internal administration.

The new method, he states, is of special value for the treatment of gall-stone and renal colic, of cardialgic paroxysms, of attacks of asthma and angina pectoris. Injections of morphia, hitherto usually given during colic, had the disadvantage of paralysing peristaltic contraction, of lessening the secretion of urine, and therefore of complicating the original disorder in an undesirable way. Antipyrin, having no such secondary effects, and yet being able to allay pain, is therefore much preferable to morphia in the treatment of these diseases.

In affections of the heart, accompanied with much pain, as in angina pectoris, and in asthmatic attacks, Antipyrin did exactly what morphia does, without having any depressing influence on the blood circulation.

According to Germain Sée, Antipyrin will take the predominating position hitherto held by morphia. Morphinism, that much-dreaded evil, is likely to diminish with the increasing use of Antipyrin.

**Du traitement des maux de tête** (cephalées, migraines névralgies faciales) par L'ANTIPYRIN. Par GERMAIN SÉE (*Bull de l'Acad.* 3 XVIII., N. 34, p. 259).

The otherwise very obstinate cephalalgia adolescentium was successfully overcome by Antipyrin. In 12 cases the headache lessened after two to three days (30—45 grains—6 to 9 Tabloids—Antipyrin per day) and completely disappeared after a six to eight weeks' treatment.

Forty-two patients afflicted with migraine took 15 grains (3 Tabloids) of Antipyrin on awakening, 15 grains (3 Tabloids) one hour



later. The paroxysms were thereby checked, sometimes a second dose being unnecessary. The attacks became much rarer when the use of the drug was continued for some time. In four of the cases the treatment had to be interrupted, the following ill-effects being caused: indigestion twice, vertigo once, congestion in the head once.

Of seven cases of neuralgia of the fifth nerve one remained uncured, two were completely cured, and in the other four cases, which had existed for years, a marked improvement took place after two months' treatment (daily dose: 75 grains internally and 10 grains subcutaneously).

**Sur diverses applications Thérapeutiques de l'Antipyrin, Comparaison avec l'Antifébrin.**—Par GERMAIN SÉE (*Union Med.* 111, 112. *Bull. de l'Acad. de Med.* 35 XVIII., N. 36, p. 340, 1887).

Antipyrin has proved a very efficacious drug in the treatment of articular rheumatism. In cases with high fever, salicylic acid, it is true, seemed to do more good; but even in these cases Antipyrin is preferable when the heart has become weakened. In the very chronic form of rheumatism, in arthritis sicca, and in gout, a material improvement was repeatedly observed on treatment with this remedy.

Lumbago, intercostal neuralgia, sciatica, were successfully treated by the combined method (internal and subcutaneous administration). Of 23 cases of sciatica, only two resisted the treatment. The same had occurred with all other drugs.

The different forms of neuritis and neuralgic pains of diabetes and herpes zoster are not altered in their course by Antipyrin, only the "outcry of nature is stopped." Germain Sée in all these cases prefers Antipyrin to Antifebrin, because of its complete harmlessness. The only thing which does sometimes occur after Antipyrin has been given for some weeks, is a slight urticaria, or other eruption, which however does not signify anything compared to the formation of methæmoglobin in the blood caused by Antifebrin.

With regard to the treatment of urinary calculus and renal and



gall-stone colic, the author confirms what he has stated in a former communication. (*Comptes rendus CV.*, 2.)

Dysmenorrhœa, acute metritis, different intestinal colics, were also greatly benefited by Antipyrin.

The author concludes with a few remarks on the pains attached to diseases of the heart and great vessels. Antipyrin does not alter the course of atheromatous processes of the arterial wall, but the attack of angina pectoris, which frequently is a consequence of such morbid changes, is certainly lessened by the drug, especially if it is given in the form of subcutaneous injections. Pains arising from aneurysm are also decidedly alleviated by a continued course of Antipyrin.

**Antipyrin in Otalgia nervosa.**—The many different forms of neuralgic pains of the ear are greatly lessened by Antipyrin, as was first stated by GOMPERZ, at the Eighth Meeting of German and Swiss Aural Surgeons, held at Vienna (*vide Archiv. für Ohrenheilkunde XXV.*, 1 and 2, 1887.)

**On the use of Antipyrin in diseases of the nervous system.** By Prof. MENDEL, Berlin. (*Ther. Monatshefte*, 1887. Heft 7.)

For the last twelve months the author has treated different diseases of the nervous system with Antipyrin, and his verdict on this new field for Antipyrin is :—

In most cases of migraine the attacks are shortened, and do not recur with the former frequency. The effect is similar to that of bromide of potassium or salicylic acid. In cases of neuralgia of the fifth nerve, sciatica, and neuralgic affections of the occipital nerves, a very beneficial effect was obtained. Also organic lesions of the nervous system were in many instances favourably influenced by Antipyrin; disturbances of sensation and “lightning pains” of tabetic patients, and the frightful pains in the head, accompanying severe cerebral affections, are decidedly lessened by the drug.

Antipyrin is inefficacious in epilepsy, uncertain in hysteria, where it often develops unpleasant after-effects, such as disturbances of digestion, general malaise, heart palpitation, and skin

eruptions. The favourite dose was 15 grains thrice daily, but even larger doses were readily borne.

**Antipyrin as an Anodyne in cases of Locomotor Ataxy.** By C. W. SUCKLING. (*Brit. Med. Journal*, 18 June, 1887).

The author confirms the favourable reports of Sée and Lépine on the alleviating effect of Antipyrin in cases of locomotor ataxy. In three cases of ataxy of long standing, the "lightning pains" entirely disappeared for a very long time, after only two doses of 10 grains (2 Tabloids) each had been given.

**On Antipyrin as a Nerve Tonic and Anodyne.** By Dr. SEIFERT. (*Centralbl. für klin. Med.*, 1887, N. 35).

The author first reports on the daily increasing voluminous literature on the above subject. He subsequently speaks of his own experience. The different forms of headache and neuralgic pains of the head and face were all mitigated by the drug.

**On the Subcutaneous Injections of Antipyrin in all kinds of diseases associated with physical pain.** By Dr. S. FRAENKEL, of Breslau. (*Deutsche med., Wochenschrift*, 1887, N. 41).

The author, upon the strong recommendation of Germain Sée, extensively applied Antipyrin by the subcutaneous method; the results were excellent; all kinds of physical pain disappeared. In fact, the drug never failed. He found that 5 grains (1 Tabloid) *i.e.* half the dose indicated by Germain Sée, is sufficient for causing an anæsthetic area of six to seven cm. diameter. If it is desirable to extend the anæsthetic effect over a larger surface, it may be appropriate to make several injections, no ill-effect being produced. The injection is made at the place where the greatest pain is felt.

The author treated in this way with remarkable success cases of acute, subacute and chronic rheumatisms of joints, lumbago, sciatica, intercostal, supra and infraorbital neuralgia and pleuritic pains of anæmic origin. In many cases the remedy not only acted symptomatically, but at the same time it attacked the morbid process itself. The anæsthetic effect lasted for at least six to eight hours, and passed off gradually, but the pains never afterwards returned with the former intensity.

Analgetic effect is likewise produced in many diseases of internal organs, such as otitis media, parametritis, gastralgia, cholelithiasis, asthma, &c.

A girl of five years, suffering from perityphlitis, had such frightful pains that her state was most deplorable. After injection of 5 grains (1 Tabloid) of Antipyrin the pain was nearly extirpated. Narcotics were of course undesirable for such a youthful patient, so that Antipyrin was all the more appreciated.

Unpleasant after-effects were not observed in a single case.

The author thinks that in future Antipyrin injections will largely be administered where formerly morphia was given. The new method will no doubt be frequently resorted to by the general practitioner, as it will contribute to his own credit and to the comfort of his clients.

**Antipyrin and Antifebrin**, as new anæsthetics for ophthalmic practice. By Dr. STRZEMINSKI (*Gaz. lekarska VII.*, N. 41, 1887).

The author used Antipyrin in 125 different painful affections of the eyes (10—15 grains—2 to 3 Tabloids—once or twice daily). Neuralgic pains of the eye were specially benefited. Inflammatory affections took a milder course when treated with Antipyrin. Only in cases of hysteria did the remedy not act well.

Subcutaneous application is to be preferred when rapid action is desirable.

**Laget** (*Comptes rendus de la Société de Biol.*, 1887, N. 42) gave Antipyrin for painful labours during abortion of a five months' fœtus. Two enemata, each consisting of 30 grains (6 Tabloids) of Antipyrin, dissolved in three ounces of water, had the effect of making the labours quite painless, without in the least affecting their energy.

**On the Subcutaneous Injection of Antipyrin.**—By Dr. RAPHAEL HIRSCH, of Hanover (*Berlin klin. Wochenschrift*, 1887, N. 46).

The author was induced, by Germain Seé's and Fränkel's communications, to try the subcutaneous application of Antipyrin in different painful affections. The results obtained surpassed all

expectations. Even cases which had resisted all other remedies were most effectively benefited by this new method. Acute and chronic rheumatism of joints and muscles, facial neuralgia, cardialgia, asthma, were treated most successfully. The pains usually disappeared in 1—10 minutes after injection.

After use, the syringes employed for injection should be rinsed with a five per cent. solution of carbolic acid, until the latter ceases to turn turbid. By this process the syringe is disinfected, and stopping of the needle by Antipyrin crystals is effectually prevented.

**Antipyrin against Sea-sickness.**—By DUPUY (*Le progrès méd.*, 1887, N. 48).

The too-well-known symptoms of sea-sickness, nausea, vertigo, cold sweats, vomiting, are probably caused by a state of over-excitability of the nervous system, especially the medulla oblongata. It is, therefore, comprehensible that Dupuy tried to obviate sea-sickness by the latest nerve-tonic. He recommended his "patients" to begin the treatment two to three days before going on board ship, taking 15 grains (3 Tabloids) three times each day, continuing this treatment during the first three days of sea-voyage. The success was complete. The same persons who on former occasions had suffered most intensely from sea-sickness, crossed the ocean, thanks to Antipyrin, without any appearance of the distressing complaint.

**The treatment of Chorea with Antipyrin.**—By LEGROUX *Bull. de l'Académie de Médecine, Paris*, 27th Dec., 1887).

The results which Legroux obtained with Antipyrin in the treatment of chorea were extremely favourable. A boy of  $3\frac{1}{2}$  years, who suffered from incessant convulsions, was cured by Antipyrin within 9 days (45 grains—9 Tabloids—daily). A girl of  $4\frac{1}{2}$  years was cured within 18 days; another within 10 days. A girl of 10 years was cured within 20 days, after having taken a total quantity of 2 ounces of Antipyrin. An 8 years' boy was cured after 8 days. The remedy was dissolved in orange syrup, given with or without the addition of water; 45 grains (9 Tabloids) daily were usually sufficient. The author says that Antipyrin is by far

the most efficacious and most reliable remedy in the treatment of chorea.

**On subcutaneous injections of Antipyrin.**—By R. GRÄFE (*Ber. der med. Gesellsch. zu Leipzig*, 13th Sept., 1887.)

From extensive experiments the author draws the following conclusions :—

(1) The anæsthetic action of Antipyrin, when injected subcutaneously, seems to be purely local, extending over a surface of six to ten cm. radius. With articular rheumatism the effect is different, as in this case Antipyrin acts specifically.

(2) The effect of the injection is most prominent where the pain is strictly localized, as in contusions, fractures, stiffness of the joints after prolonged immobility, inflammations, subacute articular rheumatism, arthritis deformans, if the pain is localized at certain points.

(3) Antipyrin has no effect when the pain is vague and inconstant.

(4) Also in cases of neuralgia, Antipyrin succeeds only in a limited number of instances—namely, in those where special points of intense sensibility can be made out. The effect soon passes away, or at least did so in the few cases which the author observed. It also becomes smaller and shorter with each succeeding injection, and in this respect resembles morphia. The dose has therefore to be gradually increased, if a constant intensity of action is desired.

(5) On an average the duration of the effect seems to be longer than with morphia injections. The drug has a direct curative effect in all cases where the cause of pain is attacked.

(6) It is advisable to inject just over the point of the greatest tenderness, and in the direction in which the pain irradiates.

(7) There was never any general influence observed by these local injections, nor any unpleasant secondary effects, slight burning round the point of injection lasting one or two minutes, and a sensation of numbness excepted. The latter was sometimes absent, which signified that the anæsthetic effect was lacking in distinctness.



(8) Signs of inflammation or formation of abscess were never observed, nor did any rash appear.

Only in one case of localized pain did the effect entirely fail.

Five to fifteen minims of a 50 per cent. solution was the usual dose for injection.

For cleansing purposes, the solution was repeatedly drawn through the syringe before each application. After use, the syringe was disinfected with a 5 per cent. solution of carbolic acid until the latter remained clear. It turns milky as long as any Antipyrin is left in the syringe. Any residue is likely to cause stoppage in the needle.

**On the Combination of Antipyrin and Cocaine in Dental Practice.**—By MARTIN (*Lyon Méd.* 1888, N. 7).

Concentrated solutions of cocaine injected for painless extraction of teeth frequently causes symptoms of poisoning. To avoid these the author tried to lessen the dose of cocaine and to add a small quantity of Antipyrin, according to the following formula :—

R̄ Cocaini hydrochlor gr. i.  
 Antipyrin ..... gr. x.  
 Aq. dest ..... ℥. xx.

This solution is injected between gums and tooth. The effect is quite satisfactory, sets in slower, but lasts longer than with pure concentrated solutions of cocaine.

The injection also instantly alleviates the intense pains associated with acute periosteal inflammation.

**How to allay painful labours.** By Dr. S. STEINTHAL, of Berlin. (*Deutsche med. Wochenschrift*, 1888, N. 9).

Following Laget's advice, the author ordered an enema containing 30 grains (6 Tabloids) of Antipyrin in the case of a primipara, 25 years old, whose labours, having already lasted twenty hours, had become quite unbearable. Pain was gone immediately after application. The contractions of the uterus remained unaffected. A prolonged chloroform anæsthesia, which subsequently became necessary for the artificial delivery of the child, passed off without any unusual symptoms.



**Case of severe Chorea: rapid cure by Antipyrin.**

By Dr. LOURENCIN. (*Lyon Med.*, 1888, N. 11).

A girl of seven years, suffering from severe chorea, was soon after the commencement of the illness treated with daily doses of 30 grains (6 Tabloids) of Antipyrin (gr. 10 repeated every hour). After one week a decided improvement was noticeable. The daily dose was then increased to 45 grains (9 Tabloids)—a complete cure being effected in four weeks. The remedy was easily borne throughout the whole course of treatment.

**Antipyrin against Chorea.** By Dr. W. LILIENFELD, of Wittenburg, i. M. (*Ther. Monatshefte*, 1888, *Heft* 4).

The author treated a very delicate girl of nine years, suffering from chorea. The latter increased in intensity, notwithstanding judicious treatment. An intercurrent febrile disease led him to prescribe Antipyrin, 11 grains (2 Tabloids) twice daily. To his great surprise the convulsive muscular movement became decidedly less on the day following the commencement of this medication, which, continued for eight days, resulted in a complete cure.

**De l'Antipyrin et de l'acetanilide comme médicaments nervin. Comparaison avec la solanine.** Par le Docteur G. GARDA. (*Bull. gén. de Thér. LVII.*, N. 20, 1888).

The author prescribed the three remedies in a great number of appropriate cases, and arrives at the following conclusions:—

Antipyrin acts best in cases of acute articular rheumatism and recent neuralgia. In neuralgia of old standing, antifebrin (acetanilide) is preferable. Both remedies are equally valuable in cases of chronic rheumatism, and in lightning pains of locomotor ataxy.

Solanine is uncertain in cases of acute rheumatic fever, whilst in chronic rheumatism and neuralgia it acts excellently. It is most valuable in cases of increased irritability of the motor nerves, as in tremor of patients affected with multiple sclerosis.

**Patogénie et traitement du mal de mer.**—Par OSSIAN-BONNET (*Bull. de l'Académie, LII.*, N. 2, 1888).

The author prescribed Antipyrin in doses of 20—30 grains (4—6 Tabloids) against sea-sickness to 57 persons with never-failing success. He considers Antipyrin the best remedy known against

the said complaint. The dose indicated above had seldom to be exceeded. The drug was given subcutaneously, when the patients had already been sick.

Sea-sickness is, according to the author's experience, frequently aggravated by the habit of travellers to indulge in excessive eating before starting for the voyage. He, therefore, recommends moderate living, and use of saline aperients before undertaking a sea voyage.

**Studies and Experience with Antipyrin.**—By Dr. FRANZ MAHNERT (*Mittheil. d. Ver. d. Aerzte in Steiermark, XXIV., pag. 262, 1888*).

Current literature and his own extensive experience have enabled the author to give an exhaustive treatise on the action of Antipyrin, its indications, application, &c. With regard to its antipyretic qualities, the author merely reports what others have found, but he dwells extensively on the anodyne properties of the drug. In one case of severe diabetes (6.3 per cent. sugar not influenced by exclusive animal diet), Antipyrin had, notwithstanding the statements of Goenner, no effect; and Lozet's assertion, that labour pains were favourably affected without disturbing the contractions of the uterus, was also not confirmed. But the author speaks very highly of the Antipyrin treatment of neuralgia, neuritis, cephalgia, hemicrania, &c. A case of rheumatic tetanus is reported *in extenso*. Each dose of Antipyrin (per rectum or subcutaneously) caused a considerable abatement of the symptoms. The abnormal reflex irritability in cases of paralysis agitans, asthma cardiale and laryngismus stridulus was promptly removed by the drug.

A case of severe cystitis with high temperature and frequent rigors was very favourably influenced by Antipyrin. The bladder was first washed out with simple distilled water. Subsequently two to three ounces of a two to three per cent. solution of Antipyrin were injected. Rapid improvement and ultimate complete cure was the result.

The author observed a case of hæmoptoe in which, after intramuscular injection of Antipyrin, hæmorrhage entirely stopped.

However, he does not wish to draw too hasty conclusions from a single favourable case.

Undesirable after-effects were observed in one case only, where a measly rash made its appearance.

With regard to the mode of application the author proposes to distinguish between anodyne and antipyretic action. He recommends intramuscular injection of 10—15 grain (2 to 3 Tabloids) doses if the former is desired, administration by the mouth or per rectum if reduction of temperature is the main object.

**On Subcutaneous Injections of Antipyrin.**—By Dr. AUGUST WOLFF, of Breslau (*Ther. Monatshefte*, 1888, H. 6).

Antipyrin given internally has a calming influence on the whole nervous system; injected subcutaneously it produces a kind of local anæsthesia; besides, it often specifically attacks the cause of pain. He injected a solution of equal parts of Antipyrin and distilled water, inserted the needle on the spot of the greatest pain and diverted it along the line of radiation of the pain. The ordinary dose was 15 grains of Antipyrin. Half this quantity was sometimes found sufficient.

The author subsequently gives a number of histories of patients, from which it appears that muscular rheumatism, thoracic pains of consumption, asthmatic paroxysms, superficial neuralgia, form specially suitable cases for Antipyrin injections. They often successfully replace morphia injections. They may even be of diagnostic value, as for instance in rapid superficial breathing of patients suffering from pneumonia, where the injection, by alleviating pleuritic pain, may cause deeper and slower respiration.

The anodyne action of the drug sets in rapidly (after five minutes at the most) and disappears after 10 to 12 hours. The injections are free from disadvantages, only slight burning being felt at the place of injection, which, however, passes off very quickly. It may be avoided by addition of cocaine to the solution.

**De l'Antipyrin dans les maladies infantiles et le traitement de la Chorée.**—Par M. le Dr. MONCORVO, Professeur à la Policlinique de Rio de Janeiro (*Revue gén. de Clin. et de Thér.*, 1888, N. 22).

Giving first a brief résumé of his former publication (*De l'Antipyrin dans la thérapeutique infantile*, 1886), the author concludes, from more than 200 different observations, that Antipyrin forms the most powerful and least dangerous antipyretic for children; that it acts admirably in cases of acute, subacute and chronic articular rheumatisms, and that it also forms a most valuable anodyne in painful diseases of children (neuralgia, gastralgia, otalgia, &c.). The author further observed that the general malnutrition of the body after surgical operations or prolonged suppurations was decidedly improved by the use of Antipyrin; and its hæmostatic properties proved to be of great service. But nowhere was its success greater than in diseases of the general nervous system. Two most serious cases of chorea were completely cured by Antipyrin after 17 days and four weeks respectively. Both patients (of 12 and of 8 years) bore the treatment excellently; up to 90 grains (5 Tabloids) were given per day. The first signs of improvement were visible after three to four days, the convulsive movements becoming less, the appetite improved, as did also the general nutrition of the body.

**On the Action of Antipyrin in Dysmenorrhœa.**—By Dr. WINDELSCHMIDT, Köln. (*Allgem. med. Centralzeitung*, 1888, N. 53).

The author ordered Antipyrin enema (30 grains *pro dosi*) in a few cases of cramps and colic before and during the period of menstruation. The results obtained were highly satisfactory. The pains mostly disappeared half-an-hour after the enema was administered; in one case the latter had to be repeated after 12 hours. The soothing effect was accompanied with an inclination to sleep. No disagreeable complications were observed, profuse perspiration and slight ischuria excepted. A glass of wine or beer was occasionally given where a tendency to collapse manifested itself.

**On subcutaneous injections of Antipyrin.** By Dr. FRIEDRICH MERKEL. Report at the Medical Congress of Nürnberg. (*Münchener medicin Wochenschrift*, 1888, N. 32 to 33).

Following the proposals of Sée, the author used Antipyrin

injections in 75 different cases (138 injections). The injections were usually applied subcutaneously deeply into the intercellular tissue; occasionally intramuscular injection was preferred, as in cases of sciatica. The effect was positive in 60 out of 75 cases; it was permanent in 46 cases, transitory in 14 cases, lacking in 15 cases. An intense, painful sensation of burning was regularly noticed immediately after injection; it lasted 10 to 15 seconds, was followed by a sensation of dull tension and numbness; subsequently the place felt entirely painless. This last stage was of quarter to 48 hours' duration.

The author recommends injections of Antipyrin in the following instances:—rheumatism confined to a single joint, sciatica, muscular pains, pains in the chest of phthisical patients. Pain in pneumonia may be allayed by Antipyrin injections, otherwise the latter will never be able to replace the use of morphia. Internal administration is the only appropriate method where an antipyretic effect is desired.

The author finally draws attention to the recent statements of Liebreich, according to which local anæsthesia of variable duration is produced by many different substances.

**On the use of Antipyrin and Antifebrin against Head-ache.** By Dr. G. CARTER. (*The Journal of the American Med. Assoc.*, 11 Aug., 1888).

The author obtained excellent results with both remedies against head-ache. He usually ordered 5 grains (1 Tabloid) to be repeated every hour until all pain had disappeared. A considerable improvement was mostly observed after the first dose; it never failed to appear after the second.

Transitory weakness of the heart, in consequence of the Antipyrin treatment, was sometimes observed in very weak, highly chlorotic subjects.

**On Aneurysms and their Treatment with Iodide of Potassium and Antipyrin.**—By GERMAIN SÉE (*Bull. de l'Acad. de Méd. Paris*, 14 Août., 1888).

The author, after discussing the pathogenetic relation between aneurysm and tuberculosis of the lungs, deals with the different



methods of treating aneurysms. Filipuncture and electro-puncture, formerly recommended, are now generally given up. Ordinary heart tonics, except sparteine, are contra-indicated in Germain Sée's opinion. The only admissible treatment consists of the administration of iodide of potassium or of Antipyrin. The latter had great effect on the pains and neuroses caused by the pressure of the sac. Phenacetin and antifebrin cannot replace Antipyrin.

**On the Anodyne Properties of Antifebrin and Antipyrin.**—By Dr. RAPHAEL HIRSCH, Hanover (*Ther. Monatshefte*, 1888, *Heft* 10).

The author welcomes two remedies like Antipyrin and antifebrin, which are able to replace morphia in a great number of instances, and which, therefore, will largely contribute to lessen the frequency of morphinism.

By the favourable reports of G. Sée and Fränkel, he was induced to try the subcutaneous method of administering Antipyrin. Having already briefly reported on a few cases treated in such a way, he now gives the particulars of 26 different diseases. In cases of rheumatisms of the muscles or joints (seven cases), Antipyrin acted quite as a specific. Three cases of traumatic lumbago were immediately cured by 7 minims of 50 per cent. solutions injected on each side of the vertebral column.

With regard to the use of Antipyrin as a nerve-tonic, the author thinks that it is contra-indicated in cases of hysteria; also in a case of sciatica (probably of central origin) it failed to have any effect. In all other cases success was complete, and often a permanent cure was effected. The following is a short list of the successfully treated cases:—

Neuralgia of the fifth nerve, intercostal neuralgia (7); “Crises gastriques” of tabetic patients (1); cardialgia, caused by ulcer of the stomach (1); pleuritic and articular pains of anæmic subjects, perityphlitis (1); and asthma bronchiale (1).

The subcutaneous injections never caused any unpleasant symptoms or complications.

**Painless injections of Antipyrin.**—By Dr. EUGEN SACHS, (*Ther. Monatshefte*, 1888, *Heft* 10.)

As subcutaneous applications of pure Antipyrin solutions are rather painful, the author tried to avoid this drawback by previous injection of a small quantity of cocaine. He reports on three cases of unilateral neuralgia of the fifth nerve, and five cases of chronic cephalalgia, which after one to four injections of 10 grains (2 Tabloids) of Antipyrin, were permanently cured. The most important task in the treatment is to find out the "tender spots" which have to be chosen for inserting the needle.

**Un cas d'hallucinations guéri par l'Antipyrin.**—Par Dr. SALEMI, de Nice, (*Bull. gen. de Thér*, 1888, N. 44.)

A lady, 38 years old, who ever since the death of her husband, three years ago, had suffered from daily visual and aural delusions, and who showed great depression of mind, was ordered Antipyrin, 10 grains (2 Tabloids) daily. After a few days the delusions became less in intensity and frequency, and a certain self-confidence returned. All delusions and other mental symptoms disappeared after the daily dose of Antipyrin had been doubled, and the lady completely regained her former health.

**Antipyrin against laryngismus stridulus.**—By PERCEVAL (*The Lancet*, Nov., 1888).

Perceval treated a good many cases of laryngismus stridulus with Antipyrin (2 grains every hour) and was highly satisfied with the result.

**On Prophylaxis and treatment of Sea-sickness.**—By Dr. MAX COHN, in Berlin (*Ther. Monatshefte*, 1889, N. 1.)

The author, whilst holding an appointment as surgeon on board a steamer, frequently tried antifebrin and Antipyrin against sea-sickness. He gave it before as well as during the attacks; dose 10 to 15 grains (2 to 3 Tabloids). Antifebrin had no effect whatever. Antipyrin was only of little service in the prevention of sea-sickness. Where the latter had already set in, the symptoms were frequently lessened by one or two doses of 15 grains (3 Tabloids) of Antipyrin. The patients felt better, head-ache and vomiting were mitigated, and the appetite returned.

**Antipyrin in a case of suspected Snake-bite.**—By Mr. MAYNARD (*Practitioner*, December, 1889, p. 435).

Mr. Maynard records the following case from India. At 8.30 a.m., on July 11th, a small fox-terrier bitch, belonging to the author, was smelling about in the long grass, when she was seen to suddenly jump and run towards the bungalow. On examining the dog, the marks of a tooth-bite were seen on the left side of the tongue. The dog soon seemed very restless, and convulsions set in. About an hour afterwards the dog lay quite unconscious, with dilated pupils, head drawn back, and all four legs perfectly rigid; no fæces or water passing. Some whisky was given to the dog, and the temperature was found to be  $106^{\circ}\text{F}$ . Having some Antipyrin in his pocket, Mr. Maynard gave the dog ten grains in a little whisky at 9.45 a.m. At 10.15 the temperature was  $104^{\circ}\text{F}$ ., but the spasms remained the same, though the pupils were contracting. Another dose of Antipyrin was then given, and at 10.40 the temperature was  $101^{\circ}\text{F}$ . At 11 a.m. five grains more Antipyrin were given, the temperature was normal, and the dog seemed nearly well. She slept the remainder of the day, but has been quite well ever since. Altogether she had twenty-five grains of Antipyrin and  $1\frac{1}{2}$  drachms of whisky. It was unfortunate that the author could not be certain what had bitten the dog, but it was probably a snake of some sort; however, the case is very interesting, and it would be useful to follow up the value of Antipyrin in cases of snake-bite.

**Antipyrin in Migraine.**—By G. C. KINGSBURY (*British Med. Journal*, Dec. 24, 1887).

The author treated 20 cases of migraine with Antipyrin, several of them were of more than 10 years' standing. He ordered 8 grains of Antipyrin to be repeated every half-hour until complete disappearance of pain was effected. Most of the cases were cured after two, some after three doses. It failed in no case. Sweating was the only consequent symptom.

Antipyrin is therefore the most powerful remedy for migraine. It not only cuts short the actual attack, but it also prevents further attacks.

**Notes on Antipyrin.**—Read before the Oxford Branch of the Brit. Med. Assoc. by W. T. BROOKS (*Br. Med. Journal*, May 19, 1888).

The author made extensive trials with Antipyrin against migraine. In the out-patient department the remedy became a general favourite, and the results were excellent; 5—7 grains (1 to 1½ Tabloids) were given at bed-time if the attack was expected for the following morning; if it usually set in in the evening, the dose was given on the previous morning.

In bilious head-ache, after excesses in alcohol, Antipyrin acts wonderfully.

Several cases of spermatorrhoea were cured by Antipyrin, combined with chloral hydrate, 10 grains of each being given at bed-time.

The author does not hesitate to declare that the power of Antipyrin in relieving migraine and other forms of cephalalgia, is in many cases simply magical. Antipyrin forms the best anodyne known in diseases where morphia is contra-indicated, as in advanced cases of kidney diseases, acute gout, or bronchitis in old people.

Antipyrin is further indicated in cases of long-continued pain, as in locomotor ataxia, &c. With antifebrin the effect is not quite so certain as with Antipyrin.

**Antipyrin as an Anodyne in Labour.**—By SIELSKY, Surgeon to the Lemberg Hospital, Galizia (*Wiadomosci Lekarskie*, N. 10, 1888).

He tried Antipyrin in three cases of labour at full term, and in one case of abortion, and found that it was much superior to all other remedies that have hitherto been recommended for the relief of the pains of labour. Fifteen grains (3 Tabloids) were given and repeated every two hours.

### **Antipyrin in Epilepsy.**

Traty has written a thesis on this subject. He concludes that the drug has a manifest influence over some cases of epileptic convulsions. This influence is akin to that of the alkaline bromides. To obtain good results large doses (from 45 to 120 grains) must be given daily.

**Antipyrin as an Anodyne.**—By ARTHUR JAMIESON, M.D.

In a case of excruciating pains, accompanying the period of

menstruation, prompt relief was afforded by 5 grain (1 Tabloid) doses of Antipyrin repeated every half-hour.

Constant pain in left lumbar region disappeared after a few doses of the drug.

A temporal neuralgia of a barrister was more benefited by Antipyrin than by any previous medication, such as quinine and phosphorus.

**Antipyrin in Head-ache.**—By NATHANIEL EDW. DAVIES (*Lancet*, Dec. 31, 1887).

The effect of Antipyrin in cases of migraine and other forms of head-ache, due to worry and over-work, has been simply marvellous. It leaves no ill-effect whatever. The best way of administration is 10 grains (2 Tabloids) repeated every hour for two or three hours, and then at intervals of six hours for a day or two, to prevent all chance of recurrence.

#### IV.—ANTIPYRIN IN WHOOPING-COUGH.

**On the Treatment of Whooping-cough.** By Dr. DEMUTH. (*Vereinsblatt der Pfälzischer Aerzte*, 1886, N. 6).

The author draws attention to the fact that nearly all remedies hitherto recommended for whooping-cough are more or less uncertain in their effect, and frequently afford only temporary relief. It seemed therefore quite justifiable to try to obtain better results with the modern antipyretics, which are also antizymotics, and may therefore be reasonably expected to have some influence on a disease like whooping-cough, which is undoubtedly of zymotic origin. Of the different antipyretics, the author chose Antipyrin for the following reason: adults who suffered from whooping-cough and complicated catarrhal affections of the naso-pharynx and frontal sinuses, with subsequent supra-orbital neuralgia, were ordered Antipyrin, which not only cured the neuralgia but at the same time had a beneficial influence on the paroxysms of whooping, and contributed to calm the patients during the night. It was therefore only natural to try the same drug in the whooping-cough of children. The result of such treatment was the following: the



course of whooping-cough was stopped at once if the treatment was commenced at the onset. When the disease had already lasted for some time, Antipyrin often caused the paroxysms to become shorter, less severe, and less frequent. This improvement was specially apparent during the night, the sleep being less disturbed, and the children felt much better in the morning. The drug is easily borne, and never objected to by the little patients. This represents an additional advantage of the new treatment.

With regard to the mode of administration, the simple solution was preferred, the dose being varied according to the patient's age, 2 grains (about half one Tabloid) being reckoned for each year, this dose to be repeated three to four times a day; the latest evening dose to be slightly larger than the others.

**Antipyrin, a substitute for Quinine in the treatment of Whooping-cough.**—By Dr. WINDELBAND (*Allgem. med. Centralzeitung*, 1887, N. 1.)

Quinine, which is one of the favourite remedies in the treatment of whooping-cough, has the great drawback that young patients frequently refuse to take it. The author therefore tried to substitute it by Antipyrin. He did so during a severe epidemic, and obtained excellent results. The paroxysmal attacks were cut short, and the whole course of the disease seemed to have been shortened by the drug, which was readily borne, and did not give rise to any secondary effects. As a rule, the following prescription was made use of:—

R̄ Antipyrin gr. xx (4 Tabloids).

Vin tocyens.

Aq. dest aa ʒi.

Syr. flor aurant ʒii.

F. mist.

S. one table-spoonful every two hours.

**On the causes and modern treatment of Whooping-cough.**—By Dr. SONNENBERGER, of Worms (*Deutsche med. Wchenschrift*, 1887, N. 14, and *Verhandl. des VI. Congress f. inn. Med.*)

Hardly any therapeutical subject is of greater importance to the medical practitioner than the treatment of whooping-cough. It is generally acknowledged that one of the most essential points in the treatment is to place the patient under excellent hygienic conditions. The medicinal treatment comes next. But with regard to the latter opinions widely differ; some even advocate not to give any powerful drugs, and to treat symptomatically. A rational treatment may be directed towards three different prominent points: the probably bacillary infection, the catarrh of the respiratory tract, and the increased reflex irritability of the nervous system, pneumogastric and superior laryngeal nerve especially. All these morbid conditions may be attacked locally or by internal medication. The local treatment (inhalations, insufflations) is not very efficacious, besides being often inconvenient or impossible, especially in the case of very young children. To fill the sick-room with the vapours of paraffin, tannic acid, creasote, etc., or the use of compressed air, seems sometimes to be beneficial.

With regard to internal treatment, narcotics were formerly in the foreground. They certainly often do good in averting or alleviating the paroxysmal coughing. But there is great risk attached to prescribing narcotics to very young children. Bromide of sodium is uncertain in its action. Quinine, which certainly does good when given in large doses, and for a considerable time has often very unpleasant after-effects. Furthermore, it is often most difficult or impossible to administer it to very young children.

The author during the last two years observed two epidemics of whooping-cough. He treated all cases (altogether about 70—80) with Antipyrin. After the first few trials he was already convinced that in Antipyrin a remedy for whooping-cough was found which in efficacy excelled all other drugs known. To quite young children he gave only very small doses, from  $\frac{1}{8}$  grain upwards. With older children he increased the dose up to 10 and 15 grains (2—3 Tabloids). The drug, dissolved in water, sweetened by the addition of some syrup, was very easily taken and borne even by the youngest children; in many a marked improvement of appetite and general nutrition took place. The author thinks it

essential that the treatment should be continued sufficiently long, as on discontinuing too early the disease is likely to exacerbate.

The results were by far the best in those cases where the Antipyrin treatment was carried out from the onset of the disease. But even when it was begun during the latter stages of the illness a marked improvement of all symptoms was noticeable. In the cases where Antipyrin was given throughout the whole illness, the latter lasted three to five weeks, and was of a very mild character : on an average six to seven paroxysms day and night. Given at the latter stages of the disease, Antipyrin caused the paroxysms to become milder and to appear less frequently.

Unpleasant after-effects did not occur. It will require further researches to find out the way in which this beneficial influence of Antipyrin is effected.

**On the specific treatment of Whooping-Cough with Antipyrin.**—By Dr. SONNENBERGER, Specialist for Diseases of Children, in *Worms* (*Ther. Monatshefte*, 1888, *Heft* 8).

The author first reviews the current literature on the subject, to which he has already contributed several communications. Antipyrin has been introduced into the treatment of whooping-cough because the administration of the probably equally efficacious quinine to young children is associated with a great many disadvantages. Quinine, being of bitter taste, being soluble with difficulty, causing unpleasant after-effect, especially on prolonged use, is not a suitable remedy for children, and will therefore be of very limited importance in the treatment of whooping-cough. In Antipyrin, however, a most excellent substitute for quinine has been found, and all the disadvantages of the latter are thereby avoided. Antipyrin is easily borne by the stomach ; it is readily taken by children when sweetened with syrup, and with cautious use never gives rise to any unpleasant secondary effects ; only small doses are necessary. The author thinks that at last a specific for whooping-cough has been found in Antipyrin.

The suitable dose varies according to the age of the young patient, one-sixth of a grain being given up to one month, two-sixths of a grain up to two months, etc., two grains to a one year-

old infant, four grains to a two year-old infant, etc. This dose is repeated three times a day, and continued until all paroxysms are entirely stopped; even then it is advantageous to continue reduced doses for another week or two. The earlier this treatment is commenced the better for the patient. The typical paroxysms sometimes entirely fail to appear when treatment has been begun very early. In the latter stages of the disease the fits become milder and rarer, which forms one of the strongest arguments in favour of the drug. It is probable that this beneficial influence of Antipyrin has to be explained by its calming effect on the nervous system, and not by its antipyretic properties, because Antifebrin, which acts similarly on the temperature, has no effect whatever in whooping-cough. It is not unlikely that a specific influence on the causation of the disease plays also an important part besides the neurotic effect.

**Whooping-cough and Antipyrin.** Par le Dr. DUBOISQUET-LABORDERIE, Saint Quen. (*Bull. de Thér. LVII.*, N. 18, 1888).

The author's experience with regard to the treatment of whooping-cough with Antipyrin, is extremely favourable; 11 out of 15 patients were cured in the course of 12 to 16 days; two children died of capillary bronchitis; in one case Antipyrin failed, in another it had to be discontinued, as the gastric functions suffered. Otherwise there were no disagreeable after-symptoms.

The remedy was given as solution in water, with the addition of syrup. The dose was 5 to 15 grains (1 to 3 Tabloids) daily for children up to two years; 15 to 60 grains (3 to 12 Tabloids) daily for older children and adults. A child who showed persistent disinclination for Antipyrin had it given per rectum.

**Remarks on the treatment of Whooping-cough with Antipyrin.**—By Dr. CROZER GRIFFITH (Paper read at the College of Physicians of Philadelphia, 1888. *Therapeutic Gazette.*)

The author was induced by Sonnenberger's communications to try Antipyrin against whooping-cough. He gave it in 15 different cases, and entirely confirms Sonnenberger's favourable statements. The effect was most remarkable when Antipyrin was given immediately after the onset of the disease. But even during the course

of illness a favourable influence was manifest, the paroxysms being shortened considerably. In one case only the effect of Antipyrin was not very prominent, although even in this case the illness was decidedly shortened.

#### V.—ANTIPYRIN AS A HÆMOSTATIC.

**Études thérapeutiques sur l'Antipyrin.**—Par HENRI HUCHARD, Médecin de l'hôpital Bichat (*Bull. de la Société de Therap. Paris*, 1885).

Huchard, who made very minute studies respecting the different effects of Antipyrin, recommends Antipyrin suppositories for hæmorrhoids. The success of the drug in this complaint is probably based on its hæmostatic action, which was found out by Hénocque and Ardain.

**L'antipyrin como emostatico.**—By EUGENIO CASATI, Ricorone (*Raccoglitore Med.* 1885, 30 Agosto, p. 153).

The author reports on his experience respecting the hæmostatic action of Antipyrin. Bleeding from the nose was at once stopped by sniffing a five per cent. solution of Antipyrin. Hæmorrhage from wounds after operations were checked within a few minutes by the application of cotton wool dipped into a four per cent. solution.

**Antipyrin as a hæmostatic.**—By OLIKHOW, (*Rousskoia Medicina*, 1887, Septbr.)

The author found that Antipyrin proved very efficacious in cases of severe hæmoptysis. He ordered frequent spraying of a solution of 30 grains (6 Tabloids) of Antipyrin in six ounces of water. This treatment not only checked the hæmorrhage, but at the same time reduced the excessive temperature.

**Antipyrin against Ulcerated Piles.**—By Dr. T. SCHREIBER, Aussee-Meran, (*Ther. Monatshefte*, 1888, Heft 7).

Neudörfer's publications on the anodyne and antiseptic properties of Antipyrin led the author to try this remedy in a case of extremely obstinate ulcerated piles, which had resisted all previous treatment. Discharge, bleeding, and intense itching constituted the most prominent symptoms. The ulcerated parts were daily



dusted with pure Antipyrin, which, later on, was applied every second day. The effect of such treatment was surprising. Pains and itching soon disappeared, the patient was able to sleep again, and the ulcers were completely and definitely cicatrized in the course of 20 days.

**Société de Thérapeutique** (Paris).—Meeting of the 11th January, 1888 (*Le Progrès Méd.*, 1887, N. 7).

Hénocque reports on the hæmostatic properties of Antipyrin, which he considers indicated in all cases of epistaxis, metrorrhagia, and hæmorrhage from superficial wounds. As regards the treatment of hæmoptysis, Hénocque confirms Moutard-Martin's statement, that the internal administration of Antipyrin has no effect on the hæmorrhage. Catillon frequently observed that hæmorrhage from small incised wounds was immediately stopped by spreading Antipyrin over the surface.

## VI.—ANTIPYRIN IN A FEW OTHER DISEASES.

**Antipyrin an excellent Stimulant for Atonic Ulcers of the Leg.**—By BOSSE, of Domnau (*Berl. klin. Wochenschr.*, 1886, N. 33).

In a case of hæmorrhage from an ulcer of the leg, Antipyrin, spread on a piece of cotton wool, was applied. After a few days, on removal of the cotton wool, it was seen that the place was covered with splendid healthy-looking granulations. The author now spread Antipyrin over the whole ulcerated surface, which possessed the size of the palm of the hand. After 10 days this large surface was covered with solid granulations, and after 22 days the ulcer had completely healed by the aid of an ointment containing two per cent. of nitrate of silver.

A similarly successful treatment was carried out in 29 other cases.

The application of Antipyrin, which was repeated every day, caused considerable pricking and burning pains, which lasted for 5 to 15 minutes. This pain disappeared as soon as the drug had

become liquified. It was considerably lessened by previous application of cocaine.

Signs of inflammatory reaction were never observed. In all cases where inflammatory signs existed already, and the ulcer was very painful, the extremity œdematous and the ulcers covered with sloughs and fœtid discharge, it was found better to advise absolute rest and to begin the treatment by disinfectant and soothing applications. When all signs of inflammation had disappeared, Antipyrin was dispersed over the ulcers.

When, after using Antipyrin, the granulations have become solid and abundant, treatment with various ointments, esp. arg. nitrate ointment, is recommended.

**Antipyrin in Diabetes.**—By Dr. GÖNNER (*Corresp. Blatt für Schweizer Aerzte*, 1887, N. 19).

The author tried Antipyrin in a diabetic patient, 60 years old. The amount of sugar in the urine had been reduced by previous treatment from 6 per cent. to 2.98 per cent. Trommer's test for sugar became indistinct after 130 grains of Antipyrin. After ten days of Antipyrin treatment (45 grains—9 Tabloids—per diem) the urine became entirely devoid of sugar.

**Antipyrin against Corneal Spots.**—By Dr. ADOLF ALDOR, of Nagy-Károly (*Orvosi Heti Szemle*, 1888, N. 18).

The author's experiments with regard to the treatment of chronic corneal infiltration reach back as far as 1885. The remedy was dusted into the eye like calomel. It causes temporary photophobia and intense burning, which lasts for one to two minutes, and is accompanied by increased lachrymal secretion. Signs of inflammation may be the consequence of too frequent applications. Cautious treatment, however, causes rapid disappearance of the infiltrations.

**Antipyrin, an anti-galactogogues remedy.**—By Dr. SALÉMI (*Bull. gén. de Thér.*, June, 1888).

The author achieved great success in prescribing Antipyrin against excessive secretion of milk. After all other medications had failed he gave Antipyrin, 9 grains (nearly 2 Tabloids) per diem, divided into three doses of 3 grains each. The secretion of

milk was diminished on the first day and entirely stopped on the third day.

## VII.—PHYSIOLOGICAL ACTION OF ANTIPYRIN.

**Sull' azione fisiologica dell'Antipirina.** By FRANCESCO COPPOLA. (*Riv. di chim. Med. e farm.*, 1884, p. 448).

As Filehne's results of his experiments on animals have never been published, this communication represents the first report on the physiological action of Antipyrin. According to Coppola, Antipyrin given to frogs in doses of one-third to two-thirds of a grain stimulates the reflex irritability of the spinal cord. Given in doses of 1 to  $1\frac{1}{3}$  grains, it excites the motor cerebral centres, causing tetanic convulsions, lasting over 24 hours. Given in still larger doses, it paralyzes the motor centres without previous excitation. Locally, at the place of subcutaneous application, it causes lessening of the sensibility; the pupils become dilated by excitation of the sympathetic nerve. The heart remains uninfluenced, and stops in diastole only after the centres of the spinal cord and medulla oblongata have become paralyzed.

**Contributions on the Physiological and Therapeutic action of Antipyrin.** By R. DEMME, of Bern. (*Fortschritte der Med.*, 1884, N. 20 and 21).

The author reports on a great number of experiments made with Antipyrin on frogs and rabbits. Rapid poisoning in cold and warm blooded animals by large doses, is effected through paralysis of the heart. Administration of smaller but still poisonous doses (half-grain with frogs, 10 grains with rabbits), causes alterations of the central nervous system; first, excitation of the different centres in the brain, medulla and spinal cord is observed, followed by paralysis.

The initial excitation of the central nervous system implicates the musculo-motor as well as the vaso-motor centres, and manifests itself by general tetanic contractions, and by increase of arterial pressure. Subsequent paralysis is shown by final disappearance

of reflex excitability, and by continuous decrease of arterial pressure, although the heart's action is not implicated.

**Contribution to the Physiological action of Antipyrin.** By Dr. R. BETTELHEIM, of Vienna, from the laboratory of Prof. v. Basch. (*Med. Jahrbücher d. k. k. Ges. d. Aerzte in Wien*, 1885, p. 263).

The author made experiments on the influence of Antipyrin on the blood pressure of curarised animals. He found that immediately after injection into the veins a depression of blood pressure is noticeable, followed by a rapid mounting; finally a definite depression is observed.

Further experiments on animals proved, that with regard to the relations of temperature each injection of a large dose is followed by an increase of cutaneous and by a reduction of rectal temperature. Increase of temperature and primary depression of blood pressure set in simultaneously, the former keeping on during the period of re-rising of the latter.

**Contribuzione alla farmacologia del gruppo della chinolina.**—By PELLACANI (*Arch. per le sc med.* VIII. 2.)

The author compares the different actions of Antipyrin, kairin, and quinine. Kairin, with regard to physiological properties, is closer allied to quinine than Antipyrin, although with regard to the antipyretic effect a nearer relation exists between Antipyrin and kairin. Both substances are unable to reduce the bodily temperature after division of the spinal cord, wherein they differ from quinine.

Kairin, in its power of destroying microbes, equals quinine. Both are able to prevent peptic and pancreatic fermentation; they facilitate the transformation of oxyhæmoglobin into methæmoglobin. These actions are not shared by Antipyrin. For frogs, kairin is twice as poisonous as Antipyrin; the symptoms are the same (central paralysis). Also for warm-blooded animals kairin is much more dangerous than Antipyrin. It kills by respiratory paralysis; Antipyrin, on the contrary, first causes excitation of the nervous centres, increased reflex irritability and convulsions. The frog's heart, when exposed after administration of Antipyrin, shows

first diminution of the quantity of blood evacuated at each systole, caused by arterial dilation; it is followed by rapid decrease of frequency and energy of the heart's action, and complete stoppage first of the ventricle, later on of the auricles. Mechanical irritation at that time still causes contractions. Kairin has the same effect; besides the latter causes transitory diastolic stoppages, which remain unaltered by camphor or physostigmine. Doses of 5 grains per kilo administered to warm-blooded animals produce unequal increase of blood pressure, with acceleration of the heart's action in the case of Antipyrin, with diminution in the case of kairin. The alterations in the frequency of pulse remain the same when larger doses are given, whilst the blood pressure is considerably lessened by intense dilation of the peripheric blood-vessels.

Quinine, Antipyrin and kairin so far closely approach each other as only very large doses cause depression of the irritability of blood-vessels and vaso-motor centre. The dilatation of peripheral vessels observed, even when only small doses have been given, is therefore caused by a direct action on the nervous centres contained in the blood-vessels. This dilatory action forms the principal base by which the antipyretic properties of the said substances have to be explained. Antipyrin does not reduce the temperature after division of the medulla; kairin does so only to a slight degree. The antithermic effect is likewise missed after division in the lower parts of the spinal cord.

Although kairin is a powerful germicide its effect in malaria is negative. The author thinks that this circumstance is to be explained by the rapid decomposition of kairin after its administration.

**Contribution à l'étude thérapeutique et physiologique de l'Antipyrin.**—Par LÉON ARDUIN, Docteur en Médecine de la Faculté de Paris (*Paris*, 1885).

Experiments, which the author made under Hénocque's direction, have proved that the blood of animals which had taken Antipyrin flowed slowly and scantily from incision wounds. These observations were followed by a series of experiments in which the author



applied Antipyrin as powder and solution to freshly-cut wounds of rabbits and guinea-pigs. Each time a rapid cessation of hæmorrhage was observed after such applications. Even bleeding from large vessels was stopped. The wounds remained dry, the edges approached each other, and rapid healing took place. Wounds made under similar conditions were not so promptly stopped by ergotin or perchloride of iron.

The author also made spectroscopic analysis of the blood. He never found any methæmoglobin after Antipyrin had been given.

Further experiments of Arduin confirm the statements made by Coppola and Demme.

**Researches on the anti-febrile action of Antipyrin and its influence on metabolism.**—By WICZKOWSKI (*Przegląd lekarski*, 1885, N. 32—35, 37—40, 43—48).

According to W. the action of Antipyrin consists of a reduction of temperature, retardation of the frequency of pulse, depression of blood pressure. Respiration remains unaffected. It has no deleterious effect on the heart. Metabolism is retarded. The quantity of urea, and also the total amount of nitrogen excreted by the urine, are diminished. The quantity of sulphuric acid bound to the different salts is diminished. The quantity of ethyl-sulphuric acid is increased. Any secretion of albumen which may have occurred previous to its medication remains unaltered. The reaction with perchloride of iron and nitric acid was distinct two hours after administration of the drug. It could still be obtained for two days after the drug had been discontinued. The chlorides are considerably diminished during the afebrile period, although chloride of sodium is increased. Antipyrin may materially shorten the course of disease. It acts as a specific in acute rheumatic fever.

**Influence of Antipyrin on the elimination of nitrogen.**—By CARL UMBACH (*Arch. f. Exper. Pathol. and Pharmacol.* XXI., pg. 161, 1885).

Ethyl-sulphuric acid in human urine is only slightly increased by the administration of Antipyrin. It is much more increased in dogs, and we may presume that the way in which Antipyrin

leaves the body varies according to the species of animal experimented on.

The author determined urea and nitrogen elimination on himself. After having balanced his in- and outcome of nitrogen, two drachms of Antipyrin were taken within two days. The temperature, accordingly, went down from 99—99.6° to 97.4—96.2°. At the beginning it caused a state of excitation and sleeplessness, followed by unusual depression. The pulse went down from 80—85 to 71.

The diminution of excretion of nitrogen amounted to 30 grains, equals 60 grains of urea, the percentage of uric acid remaining constant.

In a second series of experiments, the temperature went down from 97.6—98° to 95.6°. The other results were the same as above.

It may be concluded from these experiments that Antipyrin, like other antipyretics, such as quinine, &c., retards the general metabolism.

**The influence of Kairin, Thallin, Hydrochinon, Resorcin, and Antipyrin on the Heart and the Blood-vessels.**—By H. G. BEYER (*Amer. Journ. of Med. sc. CLXXII.*, p. 369, 1886).

The author made a great many experiments on animals, with a view of studying the antipyretic properties of the substances mentioned above. He found that Antipyrin (contrary to other antipyretics) has no deleterious influence on the red blood-corpuscles. It possesses all the necessary qualities of a first-class febrifuge remedy. It reduces the bodily temperature solely by increasing the radiation of heat. This is the consequence of considerable dilatation of blood-vessels, capillaries and small veins especially. The noxious properties of other antipyretics are not shared by Antipyrin. It acts rather as a heart-tonic than otherwise.

**The Modern Antipyretics.**—By P. T. MARTIN (*Ther. Gaz. XI.*, 5 May, 1887).

The author made a number of calorimetric experiments (with Arsonval's calorimeter), with a view of deciding the question whether the antipyretic effect of febrifuge remedies is caused by

decrease of production of heat or by increase of elimination of heat. Rabbits were chosen for these experiments. The artificial febrile temperatures were produced by wounding of the regulatory thermic centre, discovered by Ott, in the neighbourhood of the caudate body. Kairin, thallin, hydrochinon, and Antipyrin were tried one after the other. The elimination of heat was in five cases out of six increased by Antipyrin. It was diminished only in one case. Antipyrin in each case considerably reduced the production of heat.

The result is that Antipyrin forms an ideal antipyretic, as it acts in both ways—namely, by reducing the production of heat, and by increasing the elimination of heat.

**The Action of Antipyrin on the Spinal Cord.**—By CHOUPE (Meeting of the Soc. de Biol., Paris, July 2, 1887).

Choupe poisoned animals with strychnia, and at the same time injected Antipyrin. The convulsions which would otherwise infallibly have appeared were prevented by Antipyrin.

**De l'action de l'Antipyrin sur l'un des centres thermiques encéphaliques.**—Par le Docteur H. GIRARD (Rev. Med. de la Suisse romande VII, 11, 1887).

Antipyrin probably acts by directly influencing the cerebral thermic centre, situated near the caudate body. Destruction of this centre causes rising of temperature. This rising is partially prevented if Antipyrin has been given previous to the operation for destroying the centre.

**De l'Antipyrin, son action sur la nutrition, ses indications générales.**—Par ALB. ROBIN (Bull. de l'acad. de med. LI. 49, 107).

The author reports on the results of his extensive researches regarding the action of Antipyrin. This drug causes retardation of the general metabolism; it reduces the oxidation of plastic albumen. This latter influence probably forms the key-note for the anodyne properties of Antipyrin. All other anodyne remedies act similarly on the general metabolism.

According to the author, Antipyrin is also possessed of prominent antiseptic properties.

### The effect of Antipyrin on the Nervous System.

By Dr. L. BLUMENAU. (*Petersb. med., Wochenschrift, N. F., IV., N. 52, 1887*).

A dose of 10 to 15 grains of Antipyrin injected into the veins of dogs produces rapid clonic and tonic convulsions; later on, increased reflex irritability forms the most prominent symptom. These symptoms of poisoning appeared even after division of the medulla.

**Contribution to the Physiological Action of Antipyrin.**—By WERA IWANOFF, of MOSCOW, from the Physiological Institute of the University of Zürich. (*Arch. f. Anat. and Physiol., 1887, suppl.*)

The author studied the action of Antipyrin on the liver of frogs. Doses of  $\frac{1}{24}$ ,  $\frac{1}{12}$ , and  $\frac{1}{6}$  of a grain were given. Each time the liver was examined microscopically after  $\frac{1}{2}$ , 2, 6, and 24 hours respectively. The slices were stained with hæmatoxylin, nigrosin, eosin, and safranin. Half-an-hour after administration the following alterations were observed:—

The nuclei of the liver-cells were found enlarged to double or treble their normal size; their outlines were irregular; many showed ruptures, through which part of the contents had escaped. The liver-cells were often found enlarged, their protoplasm increased. These alterations were the same when larger doses were given, only the number of cells affected in the way described was increased.

Two hours after administration the liver-cells were found smaller than normal; many nuclei were pale, nearly transparent. Large doses caused slight granulation of the nuclear contents. The number of altered nuclei increased in the proportion of 1 : 1.53 : 1.83 if the dose of Antipyrin was increased in the proportion of 1 : 2 : 4.

The following changes were observed six hours after administration:—

Liver-cells of medium size, protoplasm finely granulated, stained by eosin; nuclei dark red under the influence of safranin. The nuclei show a later stage of the change observed in the second

case. Numbers of affected nuclei, increasing from 1:1.31:1.35 by increased dose 1:2:4.

In the fourth series of experiments (changes after 24 hours) a distinct recovery of the cells took place. The pole nuclei became rarer, the cells generally only slightly altered. The vessels were considerably enlarged, their volume comprising 23.6 per cent. of the volume of the whole liver, whilst in normal liver the volume of all blood-vessels made out 10.9 per cent., two hours after administration of Antipyrin 7.4 per cent., and six hours after 13.8 per cent.

The author thinks that the decay of liver-cells is a direct consequence of Antipyrin, and he believes that the antipyretic properties and the reduction of excretion of nitrogen have both something to do with this decay in the liver. He is therefore inclined to explain the antipyretic action of Antipyrin by its influence on the function of the liver, and not as other authors have done by action on the cerebral centre of heat.

**The comparative therapeutics of Antipyrin and Antifebrin.**—By ROB. PARK, M.D., Physician to the Glasgow Samaritan Hospital (*The Lancet*, 1888, page 311).

The author confirms Beyér's statements respecting the physiological action of Antipyrin. This drug causes considerable enlargement of the veins; it stimulates the energy of the heart's contractions, and has no deleterious influence either on heart or on muscles. The action of Antipyrin in disease differs from the physiological action. Vigorous patients take Antipyrin without discomfort. Weak, exhausted patients require very cautious administration if Antipyrin is indicated.

**Croonian Lectures on Antipyretics.**—By Dr. DONALD MACALISTER, Fellow and Lecturer at St. John's College, Cambridge (*Lancet*, January, 1888).

According to this able observer, Antipyrin acts in the following way:—It increases the property of radiation from the skin, it diminishes the difference between peripheral and central temperature, it lowers the temperature as a whole, diminishing thermogenesis. It diminishes metabolism, and sometimes increases



perspiration. It generally retards the heart's action, and raises slightly the tension in the radial artery. From the striking action of Antipyrin in allaying pain, it seems highly probable that it stimulates the inhibitory centres of neuro-muscular functions, which assumption also explains its action as an antipyretic.

Antipyrin in disease produces a crisis comparable to that which nature in many cases of pyrexia determines. The Antipyrin diminishes nitrogenous elimination, which distinguishes it favourably from the cold bath, which increases the elimination of nitrogen.

**Coffee a vehicle for Antipyrin.**—By Dr. BATTERBURY, Berkhamstead. (*Brit. Med. Journal*, Oct. 27th, 1888).

Dr. Batterbury, of Berkhamstead, tells us that coffee almost entirely disguises the somewhat disagreeable taste of Antipyrin. If a tabloid of Antipyrin, or its aqueous solution, be added to a cup of coffee, made with milk and sugar in the ordinary way, the mixture may be drunk without tasting the drug.

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## RECENT REPORTS.

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The decided attention which has been given to the study of the action of Antipyrin, in health and disease, demonstrates the importance of the drug in question. When first introduced the drug was considered to be simply an anti-thermic; since then, however, some hardly less important therapeutic properties have been found to belong to Antipyrin. In the first instance let us consider its remarkable analgesic properties. Antipyrin quickly relieves pain—not only that of a functional kind, but also when attended by organic disease.

In some instances Antipyrin in solution has been found to

produce a temporary urticarious rash; this is said to be due to the rapid absorption of the drug. The tabloids are, therefore, recommended as a desirable means of administering Antipyrin. One or two of these may be easily swallowed with a little water; a more gradual yet certain absorption is thus ensured, and the proper action of the drug is experienced without any detriment to the patient.

Many instances will be found recorded in the body of the work where rapid relief has been afforded in cases of migraine and ordinary headache. It has relieved aneurismal pains and those generally experienced in attacks of gastralgia. As an analgesic, Germain Sée places Antipyrin in the same class as Morphine.

### INCOMPATIBILITY.

In prescribing, it is absolutely necessary for physicians to be acquainted with a list of incompatibles. When Antipyrin is mixed with Spirit of Nitrous Ether it develops a bluish-green colour, and ultimately deposits crystals of iso-nitroso-antipyrin; this, however, is not a poisonous compound—still, where such an action is undesirable, it is advisable to avoid prescribing Antipyrin with Sweet Spirits of Nitre.

Antipyrin is incompatible with Salicylates of the alkalies; when mixed with these in powder form liquifaction takes place and, undoubtedly, decomposition occurs.

Tannic and Gallic Acids, and other astringent vegetable substances, are also incompatible with Antipyrin; when given together in solution precipitation occurs. Lead Acetate, Iron Chloride, Iron Sulphate, Copper Sulphate, are other substances which precipitate Antipyrin.

Chloral Hydrate is also incompatible with Antipyrin. An oily product results when solutions are mixed together. The compound is found to be physiologically inert.

**Antipyrin in Chronic Urticaria.**—(*Journal de Médecin*, March 10th, 1890.)

M. Nitot maintains that chronic, or at least recurrent, urticaria is essentially of nervous origin, and is relieved by drugs that act upon the nervous system. He relates the case of a girl of nervous temperament who suffered every day for some hours in the afternoon from an attack of urticaria. She had had both pain in the joints and megrim, but there did not appear to be any digestive disorder, and her diet was plain and reasonable. At first he treated her with a purgative and alkalies, but the urticaria got no better. Considering the marked periodicity of her attacks, he added Quinine to the alkalies, but no improvement resulted. This treatment was dropped, and doses of eight grains of Antipyrin were given daily, a few hours before the usual time of the attack. After the first dose the urticaria was less, and at the end of a week it completely left her, after having troubled her for more than a month. Such a result he attributes to its antispasmodic action on the nervous system, which is sometimes seen in chorea and other nervous diseases.

**Antipyrin in Whooping-Cough.**—By A. HIRSH (Orel.). *Meditzinskoie Obozrenie*, 1889, Nos. 15 & 16, p. 224. *Journal of Laryngology*, February, 1890.)

Following Genzer's recommendations, the writer tried Antipyrin (internally, 4 or 5 grains, two or three times a day) in five cases of Whooping-cough occurring to children aged from seven to eleven, and previously ineffectively treated by belladonna and other orthodox means. In every one of the patients the administration of the remedy was rapidly followed by a very marked and steady decrease in the frequency and intensity of the paroxysms, the "whoops" disappearing entirely in one or two weeks, after which complete recovery soon took place. In one of the cases the conclusive symptoms were distinctly cut short by the drug at their very commencement.—VALERIUS IDELSON.

**Antipyrin in Asthma.**—By CHARLES SMITH, M.R.C.S. (*Medical Chronicle*, March, 1890).

A man, aged thirty-six, had suffered from asthma for some years, the attacks commencing shortly after measles. The season of the year had no influence on the ailment, the paroxysms being

as frequent in summer as in winter, but the time of taking food of course had a marked influence on them.

Treatment for the purpose of preventing the asthmatic attacks entirely failed, but nitrate of amyl at first seemed to shorten them. Usually they came on every month or six weeks.

In August, 1889, thirty grains of Antipyrin were given at the commencement of a paroxysm. In ten minutes complete relief was obtained. Twenty-four hours after there was a slight recurrence of the attack, which Antipyrin promptly subdued. From that time to the present (January, 1890) there had been no recurrence of the attacks.



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